

ABSTRACTS OF WORLD MEDICINE



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ABSTRACTS OF WORLD MEDICINE

UNDER THE DIRECTION OF

HUGH CLEGG, M.A., M.D., F.R.C.P., Editor, *BRITISH MEDICAL JOURNAL*

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It is the aim of this journal to provide the reader with abstracts of all important articles appearing in medical periodicals published in every part of the world, and in this way to enable him to keep in touch with new developments throughout the whole field of medicine and in each of its special branches, including those aspects of surgery which are of particular concern to the physician.

More than 1,600 periodicals are surveyed, from which are selected for abstracting those papers which appear to make some useful contribution to the sum of medical knowledge or experience. Each paper is abstracted in sufficient detail to indicate to the general reader the nature and value of that contribution and to enable the specialist to assess its importance in relation to his own work and to decide whether the original article should be read in full. The author's own summary or an editorial summary published with the original article may occasionally be reproduced if it is suitable for these purposes, and the title and reference alone may be published in order to draw attention to a review article or other type of paper which cannot readily be abstracted.

The abstracts in each issue are grouped in sections according to subject and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together. The titles of papers written in languages other than English are given both in translation and in the original form. The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals*, as modified by *ISO Recommendation R4: International Code for the Abbreviation of Titles of Periodicals* (International Standards Organization, 1957), and in *World Medical Periodicals* (Second Edition, World Medical Association, 1957). The transliteration of authors' names from the Cyrillic alphabets is in accordance with *ISO Recommendation R9: International System for the Transliteration of Cyrillic Characters* (International Standards Organization, 1955).

Explanatory or critical comments by the abstracter or editor are enclosed within square brackets.

ABSTRACTS OF WORLD MEDICINE

VOL. 29 No. 2

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Pathology

211. Coagulation Defects Induced by Long-term Anticoagulant Therapy

P. W. BOYLES and E. S. NICHOL. *Journal of the American Geriatrics Society [J. Amer. Geriat. Soc.]* 8, 419-430, June, 1960. 8 figs., 22 refs.

The authors of this paper from Miami Heart Institute and the University of Miami School of Medicine, Florida, studied the coagulation defects occurring during long-term anticoagulant therapy in 300 patients, and correlated these with the past history of haemorrhage [of unspecified degree]. A comparison was also made with the coagulation defects observed in patients with severe liver disease.

All the oral anticoagulants employed induced abnormal thromboplastin generation—due to a relative deficiency of plasma thromboplastin component and Stuart and Hageman factors—in addition to the known effects on prothrombin conversion factors. Heparin caused prolongation of the clotting time in addition to abnormal thromboplastin generation. Patients with severe liver disease had similar coagulation defects. There appeared to be no correlation between the extent of the coagulation defects and a past history of haemorrhage; the patients were not bleeding when the tests were carried out.

A. Brown

212. Enumeration and Sizing of Blood Cells by Means of Electrical Gating

J. R. S. DOUGLAS and M. E. ATKINSON. *Medical Journal of Australia [Med. J. Aust.]* 2, 130-135, July 23, 1960. 8 figs., 5 refs.

An electronic apparatus for counting blood cells (the Coulter counter) is described in this paper from the Royal Newcastle Hospital, Newcastle, New South Wales. Blood diluted with an electrically conducting fluid (physiological normal saline) is drawn through a narrow orifice, and since the blood cells are of different electrical conductivity from the surrounding fluid the passage of each cell generates an impulse in the electric current flowing between a pair of electrodes. These impulses are fed into the counting unit, where they operate both an oscilloscope and a numerical counter. The true count has been tabulated by the manufacturer for each observed machine count allowing for "coincidence error" due to 2, 3, or even more cells passing through the orifice at the same time and being counted as one.

The authors analyse mathematically some of the possible sources of error and conclude that "the process seems to be very reliable". They state that there is no

chamber error such as that associated with flooding a counting chamber. Field error is eliminated, and statistical errors of any kind are small on account of the large number of cells counted (50,000). The method is rapid, these 50,000 cells being counted in 15 to 25 seconds. The ease of operation eliminates operator fatigue and day-to-day maintenance is negligible. Continuous inspection of the oscillograph screen provides a satisfactory working check and, further, erythrocyte size can be estimated visually from the screen, possibly as accurately as from a blood film.

H. Caplan

213. Potency of Poliomyelitis Vaccines Estimated by an Antibody Combining Test

J. G. CRAWFORD and M. F. FIELD. *Journal of Bacteriology [J. Bact.]* 80, 111-118, July, 1960. 3 figs., 15 refs.

Antibody-combining tests for estimating the potency of poliomyelitis vaccines have not been satisfactory because the amount of antigen contained in commercial vaccines is often insufficient to be measured by this procedure.

In this paper the authors describe a modified antibody-combining test which is performed in roller tubes with centrifugally concentrated vaccine. About 400 ml. of monovalent vaccine was combined with 4 ml. of 6% gelatin and centrifuged at 30,000 r.p.m. for 3 hours. The vaccine pellets were then resuspended in supernatant fluid to give a 50-fold concentration. In a grid titration, selected dilutions of type-specific poliovirus antisera were adsorbed with dilutions of the vaccine and incubated for 5 hours at 35°C. and then overnight at 5°C., the residual uncombined antiserum being then detected by the addition of a fixed amount of homologous poliovirus. By measuring the amount of non-neutralized poliovirus in each serum-vaccine dilution the antibody-combining value can be calculated. The method for calculating this and for converting the value to terms of "monkey potency" is described.

In repeated trials on the same vaccine this antibody-combining test was found to have a coefficient of variation of 23%. Comparison of the monkey potency of vaccines, as estimated by the antibody-combining test and actually determined in monkeys, showed that the coefficient of correlation for over 50 tests on monovalent vaccine pools was 0.74, with a probability of 0.001, assuming that the actual monkey-potency values were correct. The antibody-combining test never failed to indicate antigenicity in vaccine lots which were of acceptable monkey potency, while low levels of antibody-combining antigen

were observed in vaccines having little or no antigenicity for monkeys. This test may be a useful adjuvant to an animal assay.

A. Ackroyd

EXPERIMENTAL PATHOLOGY

214. Histologic Changes in the Brains of Dogs after Long-term Barbiturate Intoxication

A. B. BAKER. *Archives of Pathology [Arch. Path.]* 70, 208-215, Aug., 1960. 6 figs., 12 refs.

The effect of long-term barbiturate ingestion was studied in 16 dogs who were given 1,000 mg. of barbiturates daily for a period of 1 to 27 months. The first changes occurred at 4 months and consisted of mild swelling and chromatolysis of scattered neurons. By the 10th month, isolated nerve cells showed more severe swelling with cytoplasmic vacuolization and some nuclear changes. Minimal chronic nerve-cell alterations became apparent after the 10th month. None of these changes were prominent, and at best implicated only a few scattered nerve cells in the deeper layers of the cortex. Myelin changes were even less striking than the neuronal changes and consisted chiefly of a mild swelling and at times vacuolization of the myelin sheaths.

Because of the paucity of changes in spite of the very large doses of barbiturates, it is suggested that the usual therapeutic dose of barbiturates even when taken over a long period of time is probably not harmful to the cerebral tissues.—[Author's summary.]

215. Pathogenesis of Cerebral Vasospasm in Hypertensive Encephalopathy. I. Effects of Acute Increases in Intraluminal Blood Pressure on Pial Blood Flow

J. S. MEYER, A. G. WALTZ, and F. GOTOH. *Neurology [Neurology (Minneapolis)]* 10, 735-744, Aug., 1960. 9 figs., 16 refs.

Byrom (*Lancet*, 1954, 2, 201; *Abstr. Wld Med.*, 1954, 16, 433) mentions three possible causes of cerebral arterial spasm in severe renal hypertension: (1) excessive vasoconstriction in response to changes in intraluminal pressure; (2) a circulatory vasoconstrictor factor; and (3) abnormal irritability of the vessels in response to normal blood pressure. In an investigation carried out at Wayne State University College of Medicine, Detroit, the present authors sought to determine whether cerebral vasospasm can be produced simply by changes in intraluminal pressure without the complication of circulating humoral agents. In cats and monkeys the aorta beyond the subclavian artery was suddenly clamped, and the changes in cerebrospinal-fluid pressure and cerebral blood flow were followed with sensitive recording instruments. The responses of the pial vessels to this and other manoeuvres were observed photographically through a cranial window.

Sudden clamping of the aorta led to a rise in blood pressure in the intracranial circulation and, in response to this, a proportionate rise in intracranial pressure. The immediate response of the pial vessels was to dilate slightly for about half a minute, causing a transient increase in cerebral blood flow. This phase was immedi-

ately followed by a progressive constriction of vessels of the size of arterioles and very small arteries during the next 5 minutes, with a parallel reduction in blood flow. The calibre of the vessels was reduced by about 50%; however, the intense vasospasm seen in severe renal hypertension did not occur. Reduction in vascular diameter was not due to compression of the vessels, since it occurred with the brain exposed, and also in the exposed choroid plexus. Occasionally, after repeated severe hypertensive episodes brain swelling became very marked and a further rise in blood pressure, probably due to pressure on vasomotor centres, was noted. Death, with internal herniations of the brain, invariably followed this sequence of events.

The effects of adrenaline, ischaemic renal blood (renin), and hypertensin were also studied. Intravenous injection of adrenaline produced a transient increase in blood pressure and constriction of pial vessels. With renin there was a small rise in blood pressure and an equivalently slight constriction of pial vessels. With hypertensin a pronounced increase in blood pressure occurred and the pial vessels became markedly constricted, there being more than 50% reduction in calibre, and this persisted after the blood pressure returned to normal.

The authors consider that these changes in the calibre of the pial vessels are due to the rise in blood pressure and are physiological responses to raised intraluminal pressure. The element of vasospasm, such as Byrom saw, is absent from the present changes, and they believe vasospasm to be a pathological response. It is possible that humoral factors such as hypertensin may be responsible for vasospasm through increasing the irritability of the vascular wall.

[These beautiful experiments should be studied in the original since it is not possible adequately to describe them or convey their importance in an abstract.]

J. B. Cavanagh

216. A Correlated Histological, Cytological, and Cytochemical Study of the Tracheobronchial Tree and Lungs of Mice Exposed to Cigarette Smoke. II. Varying Responses of Major Bronchi to Cigarette Smoke, Absence of Bronchogenic Carcinoma after Prolonged Exposure, and Disappearance of Bronchial Lesions after Cessation of Exposure

C. LEUCHTENBERGER, R. LEUCHTENBERGER, W. ZEBRUN, and P. SHAFFER. *Cancer [Cancer (Philad.)]* 13, 721-732, July-Aug., 1960. 15 figs., 10 refs.

Further studies of the tracheobronchial tree and lungs in mice exposed to cigarette smoke are reported in this paper from the Institute of Pathology, Western Reserve University, Cleveland, Ohio. The smoking chamber and the methods used were described in an earlier paper (*Cancer*, 1958, 11, 490; *Abstr. Wld Med.*, 1959, 25, 147).

Of 603 mice, 243 served as controls and 360 were exposed daily to the smoke from $\frac{1}{2}$ to 6 cigarettes for periods varying from one month to 2 years. For histological examination the left main bronchus and lung were cut in "almost serial sections"; in addition, representative sections of all lobes of both lungs were taken for histological study. The deoxynucleoprotein content

of individual nuclei of bronchial epithelial cells was studied by microspectrophotometry and interference microscopy, approximately 20,000 nuclei from 200 mice being analysed.

The most striking finding was the great variability of response from mouse to mouse, ranging from "no alterations" to bronchitis associated with atypical epithelial proliferation. This suggests that there are factors in the host which must be present if cigarette smoke is to be injurious to the tracheobronchial tree. The authors discuss the possibility of viruses being such a "host factor"; they are now carrying out further experiments to test this hypothesis.

No invasive bronchogenic carcinoma was found, even in mice subjected to nearly life-span exposure. Cytochemical studies showed an early increase in intranuclear protein (before microscopical changes), followed by a gradual increase of deoxyribonucleic acid (DNA) content. These changes, it is stated, may be related to increased cell growth and division.

The effect of stopping exposure to cigarette smoke was studied in 114 mice. Of 51 which were killed after being allowed to live without further exposure for 20 to 300 days, only 4 showed severe histological changes in the bronchi, whereas of 63 mice killed immediately after exposure 17 showed severe bronchial changes. This decrease in the incidence of bronchial lesions after cessation of exposure suggests that the changes are reversible. Further, the intranuclear protein and DNA values returned to normal, indicating reversibility of the cytochemical changes after cessation of exposure. However, the authors themselves stress "the pitfalls encountered when interpreting data obtained in mice that show a variable response from mouse to mouse".

I. Berkinshaw-Smith

CHEMICAL PATHOLOGY

217. **Nitrogen Metabolism in Children and Adolescents with Congenital Heart Disease.** (Некоторые данные о состоянии азотистого обмена при врожденных пороках сердца у детей и подростков)
N. G. ZERNOV. *Вопросы Охраны Материнства и Детства* [Vop. Ohrany Materin. Dets.] 5, 23-28, July-Aug., 1960. 8 refs.

The state of nitrogen metabolism is of great clinical and prognostic significance. In the present study the blood levels of residual N and urea N were determined by Kjeldahl's and the urease method respectively (the "urogenesis coefficient" being also calculated) in 131 young patients with congenital heart disease. Since patients with renal involvement were excluded from the study the results are thus wholly referable to hepatic function.

Residual N and blood urea levels were normal in 37 of 39 patients with patent ductus arteriosus. The ratio of non-protein N and residual N, however, was over 50% in 20 of these patients, indicating latent hepatic insufficiency, and this was confirmed by the finding that the urogenesis coefficient was below 45% in 17 cases. Of 21 patients with interventricular septal defect the

non-protein N value was near the upper limit of normal in 19, this being associated with a proportional increase in urea N and residual N. The latter was over 50%, while the urogenesis coefficient ranged from 44 to 32% in 10 of the 21 patients. In other forms of non-cyanotic congenital heart disease the non-protein N and residual N levels were usually within normal limits, but in 10 of 14 patients the urogenesis coefficient was lowered, and in a few cases of Lutembacher's syndrome and patent ductus arteriosus combined with Fallot's tetralogy it was as low as 38 to 33%. Liver function, and in particular urea formation, are therefore deficient in a majority of children with non-cyanotic congenital heart disease, probably, it is suggested, as a result of haemodynamic disturbance due to hypoxaemia, in spite of the absence of frank circulatory failure.

A similar investigation of children with cyanotic heart disease indicated a diminished urea-forming capacity of the liver. This was more pronounced in severe cases of Fallot's tetralogy, in 14 out of 18 cases of which the non-protein N level was over 40 mg. per 100 ml., reaching in some cases 68 to 82 mg. per 100 ml. The main reason seems to be the rise in the level of residual N and a moderate rise in urea N. The urogenesis coefficient was below 45% in 16 patients. It was furthermore demonstrated that the rise in non-protein N was proportional to the degree of hypoxia. On the other hand the blood urea level (in absolute figures) bore no direct relationship to the degree of hypoxia.

S. W. Waydenfeld

218. **The Colour Precipitation Reaction in the Clinical Control of Endocrine Diseases.** (Цветная осадочная реакция мочи в клинике эндокринных заболеваний)
S. A. BALEN. *Проблемы Эндокринологии и Гормонотерапии* [Probl. Ėndokr. Gormonoter.] 6, 77-81, July-Aug., 1960. 18 refs.

The author reports the results obtained with Kimbarovski's colour precipitation reaction in the urine in the investigation of patients suffering from various endocrine diseases, including diabetes insipidus, diabetes mellitus, thyrotoxicosis, and simple goitre. This reaction has been employed for the early detection of acute and chronic infections, in which it has been found more sensitive and to appear earlier than the diazo reaction, the leucocytic response, and increase in the erythrocyte sedimentation rate. The technique of the test, which is simple, is as follows: 1 ml. of early morning urine is placed in each of three test-tubes, to which is then added 1, 0.75, and 0.5 ml. respectively of a 5% aqueous solution of silver nitrate. On boiling, a precipitate is formed, which varies from white (negative reaction) through lilac or pink (doubtful reaction) and coffee-coloured (weak positive) to coal-black (very strongly positive).

In healthy persons the result is always negative or doubtful. In most infectious diseases and acute or chronic infections, including brucellosis, tuberculosis, and encephalitis, the urine gives a clearly positive response. The author reports that in the endocrine diseases investigated the urine also gave a positive

response. Thus, of 241 cases of the various endocrine disorders enumerated above, none gave a negative or doubtful response on first examination, 38 were weakly positive (30 to 50%), 109 were positive (50 to 70%), 63 strongly positive (70 to 85%), and 31 very strongly positive (85 to 100%). After treatment and apparent clinical cure the responses were as follows: 3 doubtful, 54 weakly positive, 129 positive, 45 strongly positive, and 10 very strongly positive. The reaction appears to vary with the severity of the endocrine imbalance, but it is noted that in no case did the reaction become negative after treatment, showing that therapeutic restoration of the balance does not eliminate the metabolic by-product responsible for the reaction. The only exceptions were 3 out of 7 cases of thyrotoxicosis, which gave a negative or doubtful reaction 6 to 8 months after subtotal resection of the thyroid gland, and 6 out of 8 cases of simple goitre after a similar interval. *L. Firman-Edwards*

219. Plasma Insulin Concentrations in Nondiabetic and Early Diabetic Subjects. Determinations by a New Sensitive Immuno-assay Technic

R. S. YALOW and S. A. BERSON. *Diabetes [Diabetes]* 9, 254-260, July-Aug., 1960. 8 figs., 14 refs.

The authors, working at the Radioisotope Service of the Veterans Administration Hospital, Bronx, New York, prepared antibody against beef insulin in guinea-pigs. They then added human plasma to a mixture of this guinea-pig serum and of beef insulin, which was labelled with radioactive iodine. The human insulin interfered with the reaction between the radioactive beef insulin and the guinea-pig serum, the degree of competitive inhibition indicating how much human insulin was present. This method was used to assay endogenous plasma insulin concentration during the glucose tolerance test in healthy individuals and in middle-aged diabetic patients. Whereas the fasting insulin concentration was about the same in both groups, a lower immediate response of insulin secretion to glucose administration was observed in the diabetics, but after a period of time they produced actually more insulin than the control group. *H. Lehmann*

220. A Test of Pancreatic Function in Man Based on the Analysis of Duodenal Contents after Administration of Secretin and Pancreozymin

P. BURTON, D. G. EVANS, A. A. HARPER, H. T. HOWAT, S. OLESKY, J. E. SCOTT, and H. VARLEY. *Gut [Gut]* 1, 111-124, June, 1960. 8 figs., bibliography.

Pancreozymin in man as in animals appears to act as a specific enzyme stimulant. The preparations of pancreozymin used in these experiments also contain cholecystokinin, which causes the gall-bladder to contract, and a smooth muscle stimulant, possibly substance P.

The duodenal contents obtained in response to a standard dose of secretin and pancreozymin have been collected quantitatively in man and the volume and amount of bicarbonate, amylase, trypsin, and lipase measured in order to study pancreatic function. The results of 105 tests undertaken [at Manchester Royal Infirmary] on a normal group, in pancreatic and biliary

disease, and in non-pancreatic steatorrhoea have been analysed.

In localized pancreatic lesions and after recovery from acute pancreatitis, normal function is often retained. Mild functional impairment may be demonstrated only by a poor enzyme output in the post-pancreozymin fractions, while at a later stage bicarbonate output is affected and finally the volume of the duodenal contents is reduced. The secretin-pancreozymin test is most valuable, therefore, in the more chronic and advanced forms of pancreatic disease in which it gives a good assessment of residual pancreatic function. In diagnosis care must be taken in interpreting a functional test in terms of anatomical pathology.

The test has proved useful not only in diagnosis but also as a guide to treatment and an index of prognosis. —[Authors' summary.]

221. Serum Amylase and Serum Lipase Levels in Man after Administration of Secretin and Pancreozymin

P. BURTON, E. M. HAMMOND, A. A. HARPER, H. T. HOWAT, J. E. SCOTT, and H. VARLEY. *Gut [Gut]* 1, 125-139, June, 1960. 5 figs., 23 refs.

A simple evocative test has been used [at Manchester Royal Infirmary] to study pancreatic function. Serial estimations of amylase and lipase in blood serum are made at intervals up to 6 hours and again at 24 hours after injecting intravenously standard doses of secretin and pancreozymin. The results of 213 tests on a normal group, in pancreatic disease, in biliary and hepatic diseases have been analysed and compared with the results of duodenal intubation and an oral glucose tolerance test. A combined evocative test and oral glucose tolerance test provide evidence of pancreatic dysfunction in the majority of cases of cancer of the pancreas and chronic pancreatitis. The conditions of the test are described and the pathological lesions in which false positive evocative tests may be found are indicated.

The simple evocative test provides the earliest biochemical evidence of pancreatic disease in some patients with cancer of the pancreas and chronic pancreatitis. —[Authors' summary.]

222. The Nucleoprotein Complement-fixation Test in the Diagnosis of Systemic Lupus Erythematosus

R. SCALETTAR, D. M. MARCUS, L. A. SIMONTON, and L. H. MUSCHEL. *New England Journal of Medicine [New Engl. J. Med.]* 263, 226-229, Aug. 4, 1960. 26 refs.

The authors have used a complement-fixation test with crude calf-thymus nucleoprotein as antigen to detect one of the anti-nuclear factors commonly present in the serum of patients with systemic lupus erythematosus (S.L.E.). The test was performed on the sera of 600 healthy and diseased subjects at the Walter Reed General Hospital, Washington, D.C., and showed a positive result in 25 cases. Out of 10 definite cases of S.L.E. 9 gave a positive titre; the 10th case was also the only one in the group giving a negative L.E.-cell test result. There were 10 cases of suspected S.L.E. (only one of which showed a positive L.E.-cell reaction),

while 6 patients with various other diseases gave positive complement-fixation reactions, usually at low serum titres. Successful treatment of S.L.E. with corticosteroids was associated with a fall in the positive titre.

M. Wilkinson

223. Serum Mucoproteins. Practical Value of Their Determination. (Les mucoprotéines du sérum. Intérêt pratique de leur détermination)

A. VARAY and M. MASSON. *Presse médicale* [*Presse méd.*] 68, 1323-1326, July 9, 1960. 6 figs., 34 refs.

The value of estimation of the serum mucoprotein level in relation to hepatic and renal disease, infections, and malignancy is discussed in this paper from the Hôpital Beaujon-Clichy, Paris. The diagnostic significance of over 500 estimations, which included studies on 24 patients with cirrhotic and hepatic jaundice, 32 with obstructive jaundice (both intra- and extra-hepatic), 54 with cirrhosis of the liver, 27 with cancer, and 47 with nephritis, is reviewed. It is concluded that the value of the information obtained with this test in certain contingencies justifies consideration of its regular use as a laboratory diagnostic aid.

H. Harris

224. Liver Function in Patients with Elevated Serum Cholesterol or Low-density Lipoproteins

H. ENGELBERG. *Circulation* [*Circulation*] 22, 232-238, Aug., 1960. Bibliography.

Liver function tests were performed in 42 individuals with increased levels of serum cholesterol and low-density lipoproteins. The tests were normal in 39 patients; the sulfobromophthalein excretion was impaired in 3. These results indicate that disturbances in liver function are not usually involved in elevations of serum triglycerides. Other clinical evidence is discussed which suggests that the heparin lipoprotein-lipase lipolytic mechanism, but not the liver or reticuloendothelial system, occupies the initial role in the removal of alimentary fat from the bloodstream in man.—[Author's summary.]

MORBID ANATOMY AND CYTOLOGY

225. Precision in the Classification of Cirrhosis of the Liver

P. E. STEINER. *American Journal of Pathology* [*Amer. J. Path.*] 37, 21-47, July, 1960. 16 figs., 17 refs.

A classification of the various types of cirrhosis of the liver is presented. This classification agrees essentially with that established at the Fifth Pan-American Congress of Gastroenterology (*Gastroenterology*, 1956, 31, 213). Definitive special types of cirrhosis such as pigmentary, central, biliary, and parasitic are not discussed in detail. Objective precise criteria are provided, which enable post-necrotic and portal cirrhosis to be sharply defined. Portal cirrhosis has in turn been subdivided into 4 types, dependent upon whether the cirrhosis is simple or provides microscopical evidence of collapse, fat deposition, or intranodular fibrosis. Florid

cirrhosis has been shown to be characterized by definite criteria differing from those required by the classification for post-necrotic or portal cirrhosis.

The details of the criteria on which this classification is based have been derived from the records of 412 cases of cirrhosis examined in the files of the Department of Pathology, University of Chicago.

The main microscopical features of post-necrotic, portal, and florid cirrhosis are outlined as follows. In post-necrotic cirrhosis the stigmata of previous lobular collapse are always present. This collapse is identified by the juxtaposition in the fibrous scars of three or more portal tracts. Biliary-tract hyperplasia is inconspicuous except when biliary obstruction has occurred. The liver nodules, which can be classified anatomically as monolobular, multilobular, or mixed, are usually large and many of them contain regenerative liver tissue. Fat deposition is not conspicuous. Portal cirrhosis is characterized by nodules of liver tissue, some at least of which are regenerated or hyperplastic. These nodules are separated by fibrous scars or septa which give no proof of having been formed by the collapse and condensation of the hepatic stroma. They contain no abnormal collections of portal tracts or of hepatic arteries. This group can be divided into the 4 subtypes mentioned above. Florid cirrhosis is characterized by perilobular septa, from which springs an extensive but delicate intralobular fibrosis, by nodular hyperplasia, by extensive fatty degeneration, and by small foci of inflammatory cells which are seen in the lobules and in the septa.

As knowledge of cirrhosis increases, this analysis, which is based on structural changes, can be reclassified and re-interpreted. A method of precise classification is recommended so that the various types of cirrhosis seen in different parts of the world can be accurately compared.

A. W. H. Foxell

226. A Study of Lesions of the Intramural Coronary Artery Branches in Diabetes Mellitus

H. T. BLUMENTHAL, M. ALEX, and S. GOLDENBERG. *Archives of Pathology* [*Arch. Path.*] 70, 13-28, July, 1960. 21 figs., bibliography.

In this paper from the Jewish Hospital, St. Louis, Missouri, is described a postmortem study of the comparative frequency of various types of lesions of the intramural coronary arteries in 116 diabetic patients and 105 non-diabetic patients who had all suffered from severe coronary arteriosclerosis with myocardial infarction. [It is not stated whether this was the cause of death.]

Serial sections of the hearts were stained with haematoxylin and eosin, the Verhoeff-van Gieson stain, by a modified periodic-acid-Schiff (P.A.S.) technique, and by a colloidal-iron technique, while a 5th successive section was subjected to micro-incineration for the study of calcium distribution. The intramural coronary arteries were graded into three sizes: small (20 to 60 μ), medium (70 to 150 μ), and large (160 to 500 μ) and the lesions therein described under the following headings: (1) "haemodynamic" (that is, vessels showing fibrous or

fibroelastic intimal thickening); (2) atheromatous; (3) thrombotic; (4) inflammatory (for which the criteria were perivascular cellular infiltration or adventitial fibrosis, intimal fibrosis, and hyalinization); and (5) "proliferative lesions" (that is, endothelial proliferation with P.A.S.-positive fibrils). The arteries in the micro-incinerated sections were also graded according to intensity of calcification. The histological data from this study were then correlated with the clinical records, from which the diabetic and non-diabetic groups were further subdivided according to age, sex, and presence or absence of hypertension. [The criteria for the diagnosis of "hypertension" are vague.]

(1) Haemodynamic lesions of significant degree, which were more frequent in hypertensive patients, occurred mainly in the group of large vessels and with approximately equal frequency in the two groups—diabetics 47 out of 116 (40.5%) and non-diabetics 39 out of 105 (37.1%). Haemodynamic lesions, of apparently minor degree in the small vessels, were more frequent in the diabetic group (58 out of 116) than in the non-diabetic group (22 out of 105). (2) Atheromatous lesions were found in only 2 cases, despite the fact that such lesions were present in the extramural arteries of every patient. (3) Thrombotic lesions were present in 14 of 116 diabetics (12.1%) and in 12 of 105 non-diabetics (11.4%). (4) Inflammatory lesions were equally frequent in both groups, being noted in 40 of 116 diabetics (34.5%) and 36 of 105 non-diabetics (34.3%). (5) Proliferative lesions occurred very much more often in the diabetic than the non-diabetic group, and were particularly frequent in the medium-sized vessels, being present in 77 of 116 diabetics (66.4%) but in only 29 of 105 non-diabetics (27.6%). Age and hypertension had little apparent effect upon the incidence of these lesions. The calcification of the intramural arteries followed essentially the same distribution pattern as did the "haemodynamic" lesions.

The authors stress that their most significant finding was the high incidence of proliferative lesions in the diabetic group of patients and point out that these lesions are histochemically similar to those occurring in diabetic glomerulosclerosis (that is, they stain P.A.S. positive and colloidal-iron negative) and also both lesions show endothelial hyperplasia. *K. R. Gough*

227. Morphological Aspects of Interstitial Pulmonary Fibrosis

A. E. ANDERSON JR. and A. G. FORAKER. *Archives of Pathology [Arch. Path.]* 70, 79-93, July, 1960. 9 figs., 38 refs.

Pulmonary fibrosis of some degree is an almost constant postmortem finding in the lungs of adults and is a common cause of clinical disability. The present study [carried out at the Baptist Memorial Hospital, Jacksonville, Florida] is concerned specifically with the morphological features of interstitial fibrosis of different types and some normal controls, as revealed with a battery of connective tissue stains.

Alveolar walls of normal lungs consist of thin cellular membranes which are pervaded with an enormous

capillary network. They are contained within a supporting mesh of reticulin and elastic fibers. An alveolar epithelium, which is frequently seen under abnormal conditions and in the fetus, can be observed only with the aid of the electron microscope under normal circumstances. This is due to its attenuated state.

An early fibrous reaction is characterized by a proliferation of capillaries, fibroblasts and a laying down of reticular fibers. In the lungs, the capillary phase of this reaction is likely to be unusually conspicuous. The distending effects of increased pressure in the pulmonary circuit may be important in producing this appearance. As the lesion ages, the young connective tissue fibers become progressively thicker and finally assume the staining characteristics of mature collagen. Concomitantly, the cellular components and capillaries diminish and finally become inconspicuous.

Proliferation of fibrous tissue within the pulmonary interstitium may be associated with demonstrable irritants (lipoid pneumonia, silicosis, lymphangitic carcinomatosis), epithelioid granulomata of various types (sarcoidosis, tuberculosis, histiocytosis X) or obscure in nature (Hamman-Rich fibrosis, collagen disease, chronic passive congestion, interstitial pneumonia). While most of the fibrous tissue which appears to be located interstitially arises in that location, much is due to organization of intraluminal exudates on the surfaces of septa and air passages. Certain secondary changes deserve special consideration because of their frequent association with interstitial disease. These include honeycomb lung (fibrocystic disease), hypertrophy of smooth muscle, alterations of the vasculature, proliferation of alveolar epithelium and changes in the elastic framework. The presence of such features gives insight into pathogenetic mechanisms and may be helpful in identifying the basic process responsible for the fibrosis.

It is seldom emphasized that alveolar septa of emphysematous lungs are frequently the site of an interstitial fibrosis. There is an insidious replacement of the capillary bed and other alveolar contents. Some of the fibrotic septa are thickened, but most are attenuated. There is an associated disorganization of the elastic framework of alveoli, followed in turn by disruption and finally by rarefaction.—[Authors' summary.]

228. The Pathology of the Thyroid in the Syndrome of Sporadic Goitre and Congenital Deafness

J. F. SMITH. *Quarterly Journal of Medicine [Quart. J. Med.]* 29, 297-303, April [received Aug.], 1960. 6 figs., 13 refs.

The histological features of the thyroid in 14 cases of the syndrome of sporadic goitre associated with congenital deafness were studied at University College Hospital Medical School, London. Epithelial proliferation was observed in all 14 cases and was the dominant finding in 9 of them. Some colloid secretion was present in every case, while areas of fibrosis and of old haemorrhage were fairly common. In 4 cases bands of fibrous tissue were seen within the substance of the gland. The differential diagnosis of this condition from carcinoma of the thyroid is discussed. *H. Harris*

Microbiology and Parasitology

229. **The Fluorescent Antibody Technique. Its Application to Microbiology and the Arthus Phenomenon.** (La technique des anticorps fluorescents. Applications à la microbiologie et au phénomène d'Arthus) C. G. COCHRANE. *Annales de l'Institut Pasteur [Ann. Inst. Pasteur]* 99, 329-348, Sept., 1960. 10 figs., 41 refs.

230. **The Presence of a Thermolabile Antigen in Type E Flexner Dysentery Bacilli and Its Significance for the Formation of Antibodies. Part II.** (Наличие лабильного антигена у дизентерийных микробов Флекснера типа е и его значение в формировании иммунитета. Сообщение II) M. I. IGNATOVA. *Журнал Микробиологии, Эпидемиологии и Иммунологии [Zh. Mikrobiol. (Mosk.)]* 31, 48-52, June, 1960. 3 refs.

The author has shown that 33 cultures of *Shigella flexneri*, Types C, E, and F, in analogy with the Vi-antigen of *Salmonella typhi*, possess a thermolabile surface antigen which is to some extent linked with immunity to these organisms. When *Sh. flexneri* antisera were absorbed with cultures heated at 60° C. for 30 minutes they retained about half their agglutinating titre for untreated cultures. The agglutinating titre decreased to between one-quarter and one-eighth of its original value when the cultures were heated at 100° C. for 30 minutes. Analogous with the Vi-antigen of *S. typhi*, when fresh cultures were treated with alcohol the titre of the absorbed sera fell to half that obtained with untreated cultures, while no agglutination occurred with the same sera and cultures treated with hydrochloric acid. As judged by agglutination titres the content of thermolabile antigen of Types C, E, and F of *Sh. flexneri* in cultures grown for the production of vaccines in large vats under aeration was 4 to 8 times lower at the end of the usual period of growth than after 12 hours.

White mice were then immunized with vaccines which had been prepared from three strains of *Sh. flexneri*, Type E, in one of the following three ways: (1) a formalinized vaccine containing thermolabile antigen; (2) vaccine in which the thermolabile antigen had been destroyed by autoclaving at 120° C. for 30 minutes; and (3) complete antigen produced on a commercial scale, that is, in large aerated vats. Immunization with Vaccines 1 and 2 was carried out by injecting subcutaneously 2 doses of 250 million organisms in 0.5 ml., and that with Vaccine 3 by injecting subcutaneously one dose of 0.0625 mg. of a culture of *Sh. flexneri*, Type E. Ten days after immunization the mice were challenged by the intraperitoneal injection of 1, 2, and 4 minimum lethal doses (MLD) of live cultures of Type E given in 0.2 to 0.8 ml. of 0.4% nutrient agar. Protection against all 3 challenge doses was complete or nearly complete with two of the antigens (Vaccines 1 and 3), while it was also nearly complete (96.6%) with the autoclaved vaccine

(Vaccine 2) when the challenge was not greater than 1 MLD, but protection against 2 MLD was only 76.6%, and against 4 MLD only 40% (4 out of 10 mice). Similar results were obtained with vaccines of *Sh. flexneri*, Types C and F, although the immunogenicity of these types was considerably less than that of Type E.

It is concluded that the thermolabile antigen of *Sh. flexneri* strains plays an important part in the development of immunity in experimental animals.

K. Zinnemann

231. **Polyvalent Somatic Antigen for the Prevention of Staphylococcal Infection**

L. GREENBERG and M. Y. COOPER. *Canadian Medical Association Journal [Canad. med. Ass. J.]* 83, 143-147, July 23, 1960. 1 fig., 2 refs.

Previous attempts to discover an effective prophylactic against staphylococcal infections, whether in the form of a vaccine, or of antigenic fractions of *Staphylococcus aureus*, or of staphylococcal toxoids, proved mostly unsuccessful. The vaccines and toxoids protected animals only if the strains of *Staph. aureus* and staphylococcus toxins were homologous to those used for the infection. The authors have attempted, at the Department of National Health and Welfare, Ottawa, to produce a vaccine which would give protection against a large number of staphylococcal strains. To this end they prepared a polyvalent somatic antigen by combining the enzyme-lysed fractions of a number of vaccines prepared from different phage types of *Staph. aureus*, using for their investigations young hamsters and rabbits aged from 5 to 7 weeks. Before starting the experiments the animals' sera were titrated for staphylococcus agglutinins which were not to be higher than 1:32.

The results showed that only a polyvalent vaccine protected against a greater diversity of strains than a monovalent somatic antigen. Neither the whole-bacterial vaccine nor the somatic-antigen vaccine prepared from single strains was capable of protecting against a variety of strains. Animals immunized either by intramuscular or subcutaneous inoculation alone, or together with intracutaneous inoculation, survived an infection with lethal doses of *Staph. aureus* if the sera showed an agglutination titre of 1:600 or more. As the agglutination titre gave no indication of the animal's resistance to intradermal infection, it must be assumed that there was both humoral and tissue immunity. Protection against intradermal infection was obtained only when the animals were immunized both intradermally and also by an intramuscular or subcutaneous injection. The preparation of polystyrene-latex antigens from 5 separate strains of different phage types of *Staph. aureus* revealed, in agglutination tests carried out on both experimental and human sera, that all these strains had a common agglutinating antigen.

Franz Heimann

Pharmacology and Therapeutics

232. Cardiovascular Effects of Isoproterenol in Normal Subjects and Subjects with Congestive Heart Failure

H. T. DODGE, J. D. LORD, and H. SANDLER. *American Heart Journal* [Amer. Heart J.] 60, 94-105, July, 1960. 43 refs.

The haemodynamic effects of the sympatheticomimetic drug "isoproterenol" (isoprenaline) were investigated in 3 healthy subjects and 18 patients with congestive heart failure of varied aetiology. In 9 patients right heart catheterization was carried out and in a further 9 cardiac output was determined from azovan-blue dilution curves. The drug was given by intravenous infusion in a dose of 1 to 2 μ g. per minute for 15 to 60 minutes. The haemodynamic factors considered were cardiac output, ventricular work and stroke volume, systemic arterial and venous pressure and arterio-venous oxygen difference, and finally pulmonary arterial pressure and vascular resistance.

In both healthy subjects and the patients with heart failure there was an increase in cardiac output and ventricular work. The associated invariable reduction in total pulmonary vascular resistance, with insignificant changes in the mean pulmonary arterial pressure and frequent fall in peripheral venous pressure, suggested that the increase in cardiac output was due to an increase in myocardial contractility produced directly by the drug. The increase in cardiac output in the patients with congestive failure was unrelated to the concurrent administration of digitalis and indicated that the increase in myocardial contractility was of a different nature from that produced by digitalis. Additional effects of isoprenaline included a reduction in peripheral vascular resistance and in arterio-venous oxygen difference and an increase in total oxygen consumption and heart rate.

The similarity between the cardiovascular effects of isoprenaline and those of adrenaline and theophylline are pointed out. It is concluded that isoprenaline increases myocardial contractility in both healthy individuals and patients with congestive cardiac failure.

Gerald Sandler

233. A New Coronary Vasodilator Drug. Experimental and Clinical Studies. (Eine neue koronargefässerweiternde Substanz. Experimentelle und klinische Untersuchungen)

C. BÖHM, M. SCHLEPPER, and E. WITZLEB. *Deutsche medizinische Wochenschrift* [Dtsch. med. Wschr.] 85, 1405-1408, Aug. 5, 1960. 4 figs., 18 refs.

"Segontin" (N-[3'-phenylpropyl-(2')]-1:1-diphenylpropyl(3)-amine), a new substance for which coronary dilating properties have been claimed, was the subject of experimental and clinical study at the Cardiologic Institute of the University of Münster at Bad Oeynhausen. The experimental test was based on the principle that the efficiency of the coronary circulation was

a function of coronary arterial blood flow related to oxygen consumption, and was carried out on 23 dogs with unopened thorax and under general anaesthesia. A catheter introduced through the right jugular vein and reaching down into the coronary sinus was connected to an oxygen and flow meter, while at the same time arterial oxygen saturation and arterial pressure were measured by means of cannulae introduced into the femoral arteries. Segontin was given intravenously in a dose of 0.33 mg. per kg. body weight.

An increase in coronary blood flow was shown in every case 10 to 20 seconds after the injection and reached a maximum in one or 2 minutes, returning to normal values after 4 minutes. The oxygen saturation remained constant in all experiments, so that the coronary blood flow could be taken as an expression of oxygen supply. Oxygen consumption usually remained steady, but in some cases there was some slight increase. The difference between the increased oxygen supply and unchanged or only slightly increased oxygen consumption was thought to represent the improved efficiency of the coronary circulation, and is shown graphically.

These experiments were accepted as evidence of the effectiveness of the drug and a clinical trial was therefore carried out on 80 patients (77 of them men of an average age of 54 years) all of whom had been diagnosed as cases of angina pectoris and 41 (51%) of whom had evidence of previous myocardial infarction. The remaining 39 were considered to be cases of coronary arterial sclerosis without infarct. Following a control week without treatment the patients were given a 3-week course of segontin orally in a dosage varying from 10 to 30 mg. three times a day. The number and intensity of anginal attacks were taken as the criteria for therapeutic effect, and on this basis 70% of the patients without and 50% of those with previous infarct showed good or very good results; in the remainder the effects were moderate or absent. Electrocardiograms (ECG) recorded at rest and after exercise in all patients before and after treatment showed that in 20% there was evidence of improvement in the ECG tracings, without however complete correlation with subjective effects. In a double-blind trial on 50 of these patients who were given either segontin or one of two other drugs having a recognized vasodilator effect on the coronary arteries the results achieved with segontin were comparable with those of the other two drugs. In a placebo trial carried out on 40 patients subjective improvement was reported by 30% of the patients.

No toxic effects were noted and it is concluded that both clinical and experimental results show that segontin has a specific effect on the coronary circulation.

It must be stressed that in the animal experiment the drug was shown to be effective for a few minutes only, which *prima facie* is no evidence for any prophylactic effect in angina pectoris; while in the double-blind trial

the authors do not state if they themselves knew which drug was being given—an essential condition for unbiased evaluation.]

A. J. Karlish

234. Adrenocortical Steroids in the Management of Selected Patients with Infectious Diseases

W. W. SPINK. *Annals of Internal Medicine* [Ann. intern. Med.] 53, 1-32, July, 1960. 22 figs., 19 refs.

During the period 1950-9, 81 selected patients suffering from various infectious diseases were treated at the University of Minnesota Medical Center, Minneapolis, with ACTH and adrenocortical steroids in addition to other therapeutic agents. In the group of 38 patients suffering from shock and peripheral cardiovascular failure due to various bacterial infections the mortality was high (60%), but nevertheless the steroids appeared to have some beneficial effect. These patients received large intravenous doses of hydrocortisone, up to 1 g. being given in the first 24 hours, after which oral corticosteroid preparations were administered. The remaining 43 patients, who suffered from drug reactions and a variety of infective conditions in which harmful inflammatory reactions, possibly representing a type of acquired microbial hypersensitivity, were prominent, received 200 to 400 mg. of hydrocortisone intravenously in 24 hours, followed as in the other cases by oral corticosteroid therapy.

The response to this treatment was extremely good and there were no undesirable side-effects, since the treatment was continued for only a few days. It is concluded that the benefits it conferred far outweighed the possible hazards. A number of illustrative case histories are presented.

Winston Turner

235. Adrenocorticotropins and Their Use. [Monograph, in English]

H. F. WEST. *Acta medica Scandinavica* [Acta med. scand.] 166, Suppl. 352, 1-39, 1960. 34 figs., bibliography.

236. Management of Refractory Fluid Retention with a Combination of L-Arginine Monohydrochloride and Mercurials

L. I. GIDEKEL, P. SHERLOCK, A. S. PETERSON, and P. VANAMEE. *New England Journal of Medicine* [New Engl. J. Med.] 263, 221-226, Aug. 4, 1960. 1 fig., 14 refs.

The effect of mercurial diuretics in the treatment of refractory oedema is known to be enhanced by the administration of ammonium chloride, but this substance may precipitate ammonia toxicity in patients with liver disease and is also unpalatable and frequently nauseating to patients who are ill. Working at the Sloan-Kettering Institute for Cancer Research, New York, the authors found that when L-arginine hydrochloride was given to a patient with severe oedema, in an attempt to avoid the administration of an ammonium salt because of imminent hepatic coma, a massive diuresis resulted. This observation led to the trial of L-arginine monohydrochloride on 19 patients with oedema of varying causation. In 20 out of 26 trials on these patients substantial diuresis resulted, after previous administration of an apparently adequate dose of the mercurial diuretic alone had failed.

Many of the patients had severe liver disease and apparently no harm followed the use of L-arginine monohydrochloride, which was given intravenously as an 8.5% solution over a period of 2 hours, the mercurial diuretic being given intravenously either shortly before or shortly after the infusion of L-arginine.

J. McMichael

237. A Potent New Benzothiadiazine Diuretic

R. M. TAYLOR and M. M. WINBURY. *Nature* [Nature (Lond.)] 187, 603-604, Aug. 13, 1960. 7 refs.

In this communication are reported the results of experimental studies of trichlormethiazide, a benzothiadiazine diuretic agent, formed by substitution of dihydrochlorothiazide at position 3. In anaesthetized dogs the intravenous administration of as little as 1.0 µg. of trichlormethiazide per kg. body weight led to a significantly increased output of sodium and chloride in equimolar proportions. Potassium excretion also increased slightly, but considerably less than sodium and chloride excretion. In a cross-over study on 32 unanaesthetized dogs trichlormethiazide given orally was found to be 72 times more active than chlorothiazide and 13.6 times more active than dihydrochlorothiazide in promoting the excretion of sodium. The corresponding potency values for urine output were 58.9 and 7.9 respectively.

The findings suggest that the minimally effective oral dosage of trichlormethiazide in dogs is 15 µg. per kg. body weight.

Bernard Isaacs

238. Drugs which Stimulate Affective Behaviour. 3. Comparison of the Effect of Picrotoxin, Pentylene-tetrazol, Bemegride, Pipradrol, Ectylurea, Vanillic Acid Diethylamide and Deanol

A. B. DOBKIN. *Anaesthesia* [Anaesthesia] 15, 273-279, July, 1960. 21 refs.

Seven series of cross-over experiments were carried out on dogs to compare the effect of picrotoxin, pentylenetetrazol, bemegride and 4 new drugs which are used to stimulate affective behaviour. The criteria for effectiveness were: the test drug must restore breathing in the dog immediately after the injection of a fixed large dose of thiopentone, adequate breathing must persist and recovery of consciousness and ability to ambulate must be significantly faster than in the control tests (thiopentone alone). The dose of each drug that was selected after preliminary trials was one which would not cause signs of central nervous system or spinal cord irritation (twitching and convulsions) or emesis. Pipradrol was as effective as picrotoxin and bemegride but less effective than pentylenetetrazol. Vanillic acid diethylamide had no anaesthetic effect but caused marked stimulation of breathing. Ectylurea and deanol were ineffective. It is suggested that greater efficacy in the treatment of severe respiratory depression from drug poisoning and prolonged post-anaesthetic unconsciousness might be derived from combining pentylenetetrazol with one of the following: "micoren", "RP 8228" [Anaesthesia, 1960, 15, 146; Abstr. Wld Med., 1960, 28, 356], bemegride, pipradrol, or vanillic acid diethylamide.—[Author's summary.]

Chemotherapy

239. Hormonal Therapy in Carcinoma of the Breast. I. Effect of Oral Progesterone on Clinical Course and Metabolism of Nitrogen and Selected Electrolytes and Steroids

H. VOLK, G. C. ESCHER, R. A. HUSEBY, F. H. TYLER, and J. CHEDA. *Cancer [Cancer (Philad.)]* 13, 757-763, July-Aug., 1960. 3 figs., 14 refs.

Fifty-two patients with advanced breast cancer treated with hormone therapy as part of a controlled statistically randomized study are herein reported. Twenty-nine patients received progesterone, 2,000 mg. per day orally. Twenty-three patients received testosterone propionate, 100 mg. 3 times a week intramuscularly. There was no objective evidence of effectiveness of the progesterone on the advanced mammary cancers that were shown to be hormonally responsive in 8 of 19 instances when secondary therapy was used (androgens, 4 cases; estrogens, 3 cases; hypophysectomy, 1 case).

Progesterone, 2,000 mg. per day orally, is metabolically active. This dose of the drug was well tolerated with only one possible toxic reaction in the group. This agent, when administered orally in this amount, does not appear of value in the treatment of patients with advanced breast cancer.—[Authors' summary.]

240. Absorption and Excretion of Four Penicillins: Penicillin G, Penicillin V, Phenethicillin and Phenylmercaptomethyl Penicillin

C. G. MCCARTHY and M. FINLAND. *New England Journal of Medicine [New Engl. J. Med.]* 263, 315-326, Aug. 18, 1960. 8 figs., 17 refs.

In this paper from the City Hospital and Harvard Medical School, Boston, a study is reported of the serum and urine levels of the potassium salts of benzylpenicillin, phenoxymethylpenicillin, phenoxethylpenicillin (phenethicillin), and phenylmercaptomethylpenicillin in 14 healthy subjects. All the subjects received each preparation in the fasting state and again after breakfast. Both short- and long-acting preparations of benzylpenicillin were given intramuscularly and by mouth. Specimens of sera were assayed against *Streptococcus* 98, *Staphylococcus* 209P, and a *Pneumococcus* Type 3 by the two-fold dilution method and against *Sarcina lutea* by the cylinder-plate method. By far the greatest activity in the serum with greater concentration of the drug in the urine was observed after intramuscular injection of benzylpenicillin, the level in the serum being maintained for longer periods than with phenethicillin. Serum and urine levels were lower when the antibiotics were given after breakfast than when given in the fasting state, but serum levels were somewhat better maintained when the drugs were given after the meal. Of all the oral preparations tested phenylmercaptomethylpenicillin gave the highest antibacterial activity in serum and urine. Phenoxymethylpenicillin produced higher antistreptococcal and anti-

pneumococcal activity in the serum and urine than did phenethicillin, although concentrations of the latter in serum were higher. It is considered that the higher absorption and serum levels claimed for some new penicillin preparations are not reflected in a higher antibacterial activity. The problem of standards of new penicillins is discussed and the importance of expressing the activity of such preparations in terms of a standard unit such as benzylpenicillin is emphasized.

F. W. Chattaway

241. Demethylchlortetracycline

M. FINLAND and L. P. GARROD. *British Medical Journal [Brit. med. J.]* 2, 959-963, Oct. 1, 1960. 4 figs., 44 refs.

This paper reviews all the existing literature on demethylchlortetracycline (DMCT) and the results of other unpublished studies. The significant properties of DMCT are: (1) high stability; (2) an activity against most bacteria exceeding that of tetracycline (TC) by approximately twofold; and (3) a rate of renal excretion less than half that of TC, with the result that therapeutic concentrations are maintained in the blood for a much longer time after a dose.

It may be concluded from these facts that DMCT can be administered at longer intervals than other tetracyclines—two daily doses should suffice; and that a smaller dose of DMCT than of TC should achieve an equivalent therapeutic effect. Larger doses of DMCT are apt to cause diarrhoea: whether this liability exceeds that of TC is not certain.

A phototoxic reaction peculiar to DMCT may occur in treated patients exposed to bright sunlight.—[Authors' summary.]

242. Treatment of Choriocarcinoma with a Combination of Cytotoxic Drugs

K. D. BAGSHAW and J. M. McDONALD. *British Medical Journal [Brit. med. J.]* 2, 426-431, Aug. 6, 1960. 6 figs., 14 refs.

In this paper from St. Mary's Hospital and Chelsea Hospital for Women, London, a study is reported of the efficacy of cytotoxic drugs in the treatment of choriionic growths. Combinations of methotrexate (4-amino-N¹⁰-methylpteroylglutamic acid), 6-mercaptopurine, and chlorambucil were tried in 6 cases of choriocarcinoma with wide metastases, massive doses being given in courses of 3 to 5 days at intervals over 5 to 9 months. In 5 patients there was complete clinical, radiological, and hormonal remission over periods of 2 to 19 months. The remaining patient died during treatment, but this case was complicated by staphylococcal pneumonia and urinary infection; at necropsy all tumour tissue was found to be necrotic. The control of the side-effects of treatment, which were considerable, is discussed.

G. Calcutt

Infectious Diseases

243. Butadion—an Effective Drug for Combating Body Lice. (Бутадиион — эффективное средство для борьбы с платяными вшами)
V. T. OSIPJAN, V. B. KAJUDAN, and I. D. DUNAIEVA. *Журнал Микробиологии, Эпидемиологии и Иммунологии* [*Ž. Mikrobiol. (Mosk.)*] 31, 18–22, July, 1960. 6 refs.

In 1956 Mooser *et al.* reported (*Schweiz. Z. allg. Path.*, 19, 552) that they had discovered by chance that the blood of persons taking 0.6 g. of "butazolidin" (phenylbutazone) therapeutically was toxic for body lice but not for ticks, bedbugs, mosquitoes, fleas, and lice other than human body lice. In the present paper the authors confirm this finding and report that the circulating blood of persons having taken a single oral dose of 1 g. of "butadion" (a Soviet preparation) remains lethal for 92 to 100% of human body lice during the following 1 to 4 days. It is also of some epidemiological importance that body lice of the first generation which had not previously fed on normal human blood were 15 to 56% less sensitive to human blood containing butazolidin 2 to 9 days after one oral dose of 0.5 g. K. Zinnemann

VIRUS DISEASES

244. Newer Virus Diseases in Childhood

J. M. ADAMS. *Journal of Chronic Diseases* [*J. chron. Dis.*] 12, 315–325, Sept., 1960. 35 refs.

The large number of viruses which have been identified in recent years, particularly those responsible for respiratory tract diseases in children, are discussed in this paper from the University of California School of Medicine, Los Angeles. They include the myxovirus, adenovirus, and enterovirus groups, which cause various clinical patterns of illness, some confusingly similar. As the author points out it is no longer adequate to define upper respiratory infections according to the anatomical site involved; every effort should also be made to reach an aetiological diagnosis by isolation of the virus or detection of specific serological antibodies.

[This authoritative review should be read in its entirety.] D. Geraint James

245. Changes in the Serum Proteins in Botkin's Disease (Infective Hepatitis) Treated with Vitamins B₆ and B₁₂. (Динамика белковых фракций сыворотки крови при лечении болезни Боткина витаминами B₆ и B₁₂)

I. M. RASKIN and L. S. KIRŽNER. *Терапевтический Архив* [*Ter. Arh.*] 32, 72–78, July, 1960. 32 refs.

The serum proteins were investigated electrophoretically in 64 patients with Botkin's disease (infective hepatitis), in whom the disease was mild in 10 cases, moderately severe in 32, and severe in 22. Quantitative estimations were carried out colorimetrically. All the patients

received glucose, insulin, magnesium sulphate, ascorbic acid, and a special diet. In addition 26 patients (Group 1) were given 100 mg. of pyridoxine (vitamin B₆) intramuscularly daily for 20 days, and 16 patients (Group 2) 30 mg. of cyanocobalamin (vitamin B₁₂) daily for 2 days and then on alternate days up to a total of 10 to 15 injections. The control group comprised the remaining 22 patients who did not receive vitamins B₆ and B₁₂. A margin of error of $\pm 10\%$ was ignored, but an increase in the serum albumin and a decrease in serum globulin level were considered as a positive change.

A majority of patients in each group (77, 76, and 84% respectively) showed no change in total plasma proteins, but a positive change in serum albumin and globulin was observed in 72, 83, and 50% of patients in the three groups respectively. The only exception was the β -globulin level, which increased in 58% of patients in Group 1. The variations were most marked in patients with hepatitis of moderate severity. The maximum positive change was observed in the patients in Group 1, and the difference between Groups 1 and 2 in this respect was statistically significant. However, a definite positive change was observed also in Group 2. The return to normal of the protein fractions took place later in patients in both treated groups than in the control group. However, Groups 1 and 2 included more patients over 40 and more seriously ill patients than the control group, but the incidence of concomitant diseases was the same in all groups. S. W. Waydenfeld

246. Cytomegalic Inclusion Disease and *Pneumocystis carinii* Infection in an Adult

G. WILLIAMS, T. B. STRETTON, and J. C. LEONARD. *Lancet* [*Lancet*] 2, 951–955, Oct. 29, 1960. 5 figs., 36 refs.

247. Live, Orally Given Poliovirus Vaccine. Effects of Rapid Mass Immunization on Population under Conditions of Massive Enteric Infection with Other Viruses

A. B. SABIN, M. RAMOS-ALVAREZ, J. ALVAREZ-AMEZQUITA, W. PELON, R. H. MICHAELS, I. SPIGLAND, M. A. KOCH, J. M. BARNES, and J. S. RHIM. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 173, 1521–1526, Aug. 6, 1960. 5 figs., 4 refs.

In tropical areas where climatic and hygienic conditions are poor vaccination of children against poliomyelitis with consecutive doses of single types of live-virus vaccine is ineffective because of interference with multiplication of the virus in the intestinal tract from naturally occurring enteric viruses.

The present authors report the results of a field trial of mass oral administration of a single dose of trivalent poliomyelitis-virus vaccine within a period of 4 days to 86% of the 30,476 children under the age of 11 years living in the city of Toluca, Mexico. Examination of rectal swabs before administration of the vaccine had

shown that natural enteric viral infections were present within a few days of birth, the incidence reaching a peak of 72% during the first year of life. Poliomyelitis viruses were isolated from children in all age groups with a peak rate of 15% in children aged 7 months to 2 years. Although almost all the children in the city were immune to all 3 types of poliomyelitis virus by the age of 4, an average of 14 paralytic cases occurred annually. After the mass oral administration of vaccine the total incidence of enteric viral infections changed little, but poliomyelitis viruses became dominant for the first 3 weeks after vaccination, the isolation rates being as high as 70%, then rapidly declining to a level much lower than before treatment. During the first 10 weeks after vaccination conversion rates in previously negative children were 68% for Type-1 poliomyelitis virus, 82% for Type 2, and 43% for Type 3. These were much higher than the natural antibody conversion rates observed in the neighbouring city of Querataro where vaccine had not been given. In the triple-negative children, interference resulting from the simultaneous administration of all 3 types of virus with the dominance of Type 2 was clearly evident. Total infection rates appeared to be 80% for Type 1, 87% for Type 2, and 47% for Type 3. After 21 weeks negative children who were being followed up serologically were given another dose of trivalent vaccine by mouth; after this, total conversion rates were 96% for Types 1 and 2 and 72% for Type 3.

The results suggest that for the eradication of poliomyelitis in tropical regions administration by mouth of trivalent vaccine on two occasions at an interval of 6 to 8 weeks to all children under 5 years of age is a rational procedure.

A. Ackroyd

248. Vaccination against Poliomyelitis with a Live Attenuated Vaccine. (Опыт вакцинации против полиомиелита живой ослабленной вакциной) A. S. PENCİK, F. M. LISICA, and N. P. PAKALIŠ. *Клиническая Медицина [Klin. Med. (Mosk.)]* 38, 48-54, Sept., 1960. 7 refs.

The authors describe the results of a mass vaccination programme against poliomyelitis carried out in Latvia during the year 1959 with a live attenuated vaccine. As a result, during the year the incidence of poliomyelitis fell to a lower level than in any of the post-war years. Untoward reactions were few. About one in 100,000 inoculated subjects developed a clinical picture resembling poliomyelitis, but the disease could not be confirmed by the laboratory findings. Only 2 patients out of every 100,000 developed true poliomyelitis, but all completely recovered, while about one in 100,000 patients complained of transitory gastro-intestinal disturbances. A. Orley

249. Inapparent Measles after Gamma Globulin Administration

F. L. BLACK and H. YANNET. *Journal of the American Medical Association [J. Amer. med. Ass.]* 173, 1183-1188, July 16, 1960. 1 fig., 17 refs.

The authors describe the development of antibodies and subsequent immunity to measles in 19 children who had been given gamma-globulin, and who were observed

during an epidemic of measles in the Southbury Institution for Mentally Retarded Children, Connecticut, in July, 1958, and during a second epidemic in the winter of 1959. Laboratory investigations included estimation of the neutralizing and complement-fixing (C.F.) antibody titres, the Edmonston strain of virus and the Hep-2 strain of tissue culture being used. Blood specimens and throat swabs were also tested for virus by inoculation into human infant kidney-tissue cultures. The gamma-globulin used was obtained from several commercial sources, each batch having a neutralizing titre of 400 per 0.1 ml.

Altogether 119 males (aged 6 to 27 years) were at risk; they were housed in two cottages both in turn subdivided into two dormitory rooms. In the first cottage 28 individuals with a C.F. antibody titre of 4 or less were given 0.1 ml. of the globulin per lb. (0.2 ml. per kg.) body weight; of these, 7 developed modified measles. In the second cottage 19 children were given 0.05 ml. of gamma-globulin per lb. body weight; one of these developed modified measles. In the winter of 1959 a further outbreak occurred in this cottage; 30 children were given 1 ml. of gamma-globulin, and in 13 of these, who had thus had a second dose of globulin, measles developed.

None of the subjects with neutralizing antibodies in the serum developed measles, and none of these showed any immune response on further exposure. Only 5 subjects remained completely without measles antibody at the end of the outbreak. In those in whom infection was not apparent antibodies seemed first to appear coincidentally with recognition of the first overt cases. In 11 subjects (1 with overt disease) the results of tests for the presence of virus were negative. Available data suggested that children with no manifest infection or with modified disease excrete only minimal amounts of virus.

The authors point out that many children receive several prophylactic doses of gamma-globulin but never have measles. It is likely that these children develop antibody without overt disease. Determination of the C.F. antibody titre after administration of gamma-globulin may be valuable when no specific disease is manifest, a titre of 1:16 being regarded as indicating immunity.

[Although the dates and data given in the paper are confusing, this is a worth-while study and should be read in full.]

I. M. Librach

250. Immunizing Properties of Live Attenuated Measles Virus

J. DOLGIN, S. LEVINE, F. S. MARKHAM, V. CABASSO, M. WEICHSEL, J. M. RUEGSEGER, and H. R. COX. *Journal of Pediatrics [J. Pediat.]* 57, 36-41, July, 1960. 10 refs.

At Sea View Hospital, Staten Island, New York, 20 children were vaccinated subcutaneously with live attenuated measles virus, the vaccine being prepared by tissue-culture passage or from the amniotic sac of the chick embryo. It was found that susceptible children either remained asymptomatic or had a mild form of measles with fever, leucopenia, and a faint eruption. Significant

titres of neutralizing antibodies developed in the serum. There were no complications in this small series of cases.

D. Geraint James

HELMINTHIC DISEASES

251. Bephenium Hydroxynaphthoate in Treatment of Ascariasis

G. JAYEWARDENE, M. M. ISMAIL, and Y. WIJAYARATNAM. *British Medical Journal* [Brit. med. J.] 2, 268-271, July 23, 1960. 1 fig., 4 refs.

Bephenium hydroxynaphthoate ("alco-par") is active against hookworms and roundworms; it is sparingly soluble in water and has a bitter taste. The authors, from the Medical Research Institute, Colombo, Ceylon, report that they have used suspensions of uncoated or chocolate-coated granules in water or flavoured syrup in the treatment of 396 patients with roundworms, most of whom were children in State homes and orphanages in Colombo. The effect of the drug was assessed from the number of ova per ml. of faeces before treatment and 4 days afterwards. Patients in whom direct smears were negative after treatment were considered as "cleared". The object of the investigation was to determine the minimum dose of bephenium necessary for the effective treatment of ascariasis. A dose equivalent to 0.625 g. of bephenium base was insufficient; a dose of 1.25 g. gave a clearance of more than 80% of ova in 71% of cases, in some of which the initial counts were 20,000 ova per ml. of faeces or higher. With two doses of 1.25 g. given on the same day there was 80% clearance in 89% of cases. Worms were passed within half an hour of administration of the drug and were generally alive; after 24 hours the majority of the worms passed were dead and the rest only feebly active.

The only disagreeable side-effect, vomiting, which was provoked by the bitter flavour of the drug, occurred most frequently in children under 4 years of age, but the dose of 1.25 g. base could be safely given to any age group with very little vomiting. Chocolate-coated granules caused less vomiting, but were less effective than uncoated granules; they were also too bulky to be taken by the smaller children. A freshly prepared suspension of uncoated granules in a lemon-flavoured 3.5% sugar solution was the most acceptable preparation. One child who was heavily infected originally showed signs of "shock" after treatment, but recovered rapidly when the rectum was washed out and glucose given by mouth. The authors had also observed this condition after treatment with piperazine and ascribe it to the sudden release of intra-abdominal pressure which results from the evacuation of large numbers of roundworms. Wheezing, which responded to an injection of aminophylline, was observed in 2 children; this allergic manifestation is also seen occasionally after treatment with piperazine.

It is pointed out that administration of massive doses of anthelmintics for complete clearance of infection is of questionable value in countries like Ceylon where reinfection is continually occurring and there is no immediate prospect of improving the prevailing insanitary con-

ditions. The small dose of bephenium recommended by the authors for the treatment of ascariasis is effective in reducing the worm burden and can be given to patients in all age groups.

L. G. Goodwin

252. Fascioliasis in Man: an Outbreak in Hampshire

R. V. FACEY and P. D. MARSDEN. *British Medical Journal* [Brit. med. J.] 2, 619-625, Aug. 27, 1960. 3 figs., bibliography.

This paper reports an outbreak of fascioliasis which occurred in Ringwood, Hampshire, in the autumn of 1958 and in which at least 6 patients were affected, the diagnosis being subsequently confirmed in 5 by the finding of the ova of *Fasciola hepatica* in the faeces. Although 16 isolated cases have previously been recorded in Great Britain this is believed to be the first occasion on which an outbreak involving several cases of infection with this helminth has occurred in that country. The outbreak was attributed to the endemic presence of the disease in the district, in which there are many natural watercress beds, and to the unusual wetness of the summer of 1958, which acted as the precipitating factor. Clinically the illness was characterized by pain in the right hypochondrium, irregular pyrexia lasting for 6 weeks, and a marked eosinophilia. All but one of the patients presented the signs of the hepatic syndrome, 4 having hepatomegaly; the 5th patient, a woman with the respiratory syndrome probably caused by ectopic flukes, was the only patient with splenomegaly. One of the other patients probably had an ectopic fluke in the right iliac fossa, which was possibly the result of a second infection. The symptoms were quickly relieved in all cases by the administration of chloroquine, but this drug failed to kill the flukes. All the patients refused further treatment except one who had a relapse and was given two courses of emetine; this was followed by disappearance of ova from the faeces.

The initial blood studies showed a high eosinophilia, the average count being 34%, and the anaemia present in one case was thought to suggest sensitization of the erythrocytes to a circulating antibody. Electrophoretic studies showed an increase in the serum globulin level in 4 cases, while the complement-fixation test for *Fasciola* gave a positive result in all 6 cases; liver biopsy in one case showed marked infiltration of eosinophil leucocytes. Examination of the faeces was made by a modified formol-ether method, it having been found that the ordinary flotation methods did not give satisfactory results.

The conditions which must be considered in the differential diagnosis of fascioliasis include acute fevers, such as brucellosis and typhoid fever, and also other parasitic diseases. The symptoms in different cases may variously simulate Loeffler's syndrome, tropical eosinophilia, the reticuloses, or eosinophilic leukaemia. In treatment, the drug of choice appears to be emetine. In regard to prevention, the authors recommend that watercress should be grown under artificial conditions and that the inoculum should be from a healthy source, and they particularly stress the importance of control of watercress beds in endemic areas.

R. G. Meyer

Tuberculosis

253. **Prognosis of Infants Born of Tuberculous Mothers**
E. L. KENDIG JR. *Pediatrics* [Pediatrics] 26, 97-100,
July, 1960. 4 refs.

A follow-up study of 83 infants born to tuberculous mothers is reported in this paper from the Medical College of Virginia, Charlottesville. The mothers came from homes of low economic status and 72 of them were negroes. B.C.G. vaccination was given to 12 of the infants, and 3 of the remainder had no contact with their mother; none of these 15 infants developed tuberculosis. Of the remaining 68 infants, 34 became infected, 23 of whom were in contact with the mother only when the sputum was apparently negative. No other source of tuberculous infection was found in the immediate family environment.

It is concluded that separation of the infant from the mother until such time as her sputum is negative for tubercle bacilli is not sufficient to prevent tuberculous infection in the infant. B.C.G. vaccination appears to be more important.

C. M. Fletcher

254. **A Method for Studying Micro-colonial Structure and Cord Formation.** [A Survey]

J. LLOYD. *Tubercle* [Tubercle (Lond.)] 41, 281, Aug., 1960. 7 refs.

255. **The Risk of Adolescents and Young Adults Developing Tuberculosis.** (Le risque tuberculeux chez l'adolescent et le jeune adulte)

P. FRÉOUR, J. DUHAMEL, M. SERISE, P. COUDRAY, and P. CASSAIGNE. *Revue de Tuberculose et de Pneumologie* [Rev. Tuberc. (Paris)] 24, 678-693, May-June [received Aug.], 1960. 34 refs.

Many investigators in the 1930's and early 1940's showed that less clinical tuberculosis developed in that portion of the population under study who were tuberculin-positive than in those subjects who were tuberculin-negative. Working at the Tuberculosis Clinic, Bordeaux, the authors have re-investigated this problem in 2,555 final-year school-children and college students who had been tuberculin tested in 1945 and kept under observation for a mean period of 8 years. [Unfortunately 1,027 were not traced for various reasons, a fact which must raise uncertainty concerning the validity of the authors' results.]

In a series of 507 tuberculin-positive patients, clinical tuberculosis appeared in 29 (6%), whereas of the 879 who were tuberculin-negative 47 (5.8%) developed tuberculosis, a difference not statistically significant. If, however, only post-primary tuberculosis was considered, it was observed that 24 (4.7%) of 507 tuberculin-positive and only 12 of 867 (1.4%) tuberculin-negative subjects developed lesions. This latter difference is significant and suggests that post-primary tuberculosis now occurs more commonly in subjects who are tuberculin positive.

They attribute this to the much smaller risk that tuberculin-negative reactors have of becoming tuberculin positive with the present low incidence of tuberculosis in the general population.

Arnold Pines

DIAGNOSIS AND PROPHYLAXIS

256. **Complications in the Regional Lymph Nodes after B.C.G. Vaccination.** (Regionale Lymphknotenkomplikationen nach BCG-Impfung)

K. BRUNNER. *Schweizerische Zeitschrift für Tuberkulose und Pneumologie* [Schweiz. Z. Tuberk.] 17, 121-149, 1960. 3 figs., 43 refs.

An examination [at the University Pathological Institute, Zürich] of 21 cases of excised and histologically verified BCG lymphomas, with consideration of special features from the case studies and the clinical and anatomical findings, gave the following results: (1) A significant high familial incidence of tuberculosis amongst those inoculated. (2) Relatively frequent occurrence of concomitant disease or several additional, non-tubercular inoculations given rapidly during the post-vaccine phase of BCG. (3) Tuberculin allergy, in general, increased. (4) Increased occurrence of lymph node complications amongst babies and in early childhood.

(5) The typical histologic findings of a predominantly exudative caseous lymph node tuberculosis cannot be differentiated from that of a virulent infection. (6) Only in 4 cases could few acid fast nodes be demonstrated bacteriologically by a direct smear. In only one case the culture and guinea pig test were positive, with typical BCG characteristics. (7) None of the 21 cases developed a progressive tuberculosis and the local process remained absolutely benign. Finally, the author's results are brought into harmony with the present concept of the pathogenesis of the BCG lymphoma.—[Author's summary.]

257. **The Influence of the Number of Bacilli on the Development of Tuberculous Disease in Children**

D. VAN ZWANENBERG. *American Review of Respiratory Diseases* [Amer. Rev. resp. Dis.] 82, 31-44, July, 1960. Bibliography.

Since 1949 all child contacts of patients with pulmonary tuberculosis in the East Suffolk and Ipswich area have been tuberculin tested and subjected to x-ray examination of the chest. Up to December, 1956, there were 341 "index cases" which were sputum positive on direct microscopy. Altogether 305 child contacts of these cases were examined, and of these 200 (65.6%) were tuberculin positive and 71 (23%) had radiologically demonstrable tuberculous lesions. There were 171 "index cases" which were sputum positive on culture only, and of the 136 child contacts 35 (25.7%) were

tuberculin positive and only 2 (1.5%) had detectable tuberculous lesions. Finally, there were 227 "index cases" with negative sputum even on culture; of the 167 child contacts 35 (21%) were tuberculin positive and 4 (2.4%) had tuberculous lesions. These figures show not only that adults who were sputum positive on direct smear infected more than twice as many children as the other groups, but that they caused tuberculous disease in more than fifteen times as many, the differences being statistically significant. The author states that from the clinical point of view there is considerable evidence that the size of the infecting dose plays a part in deciding whether a primary tuberculous lesion in the lung of a child will be large enough to be recognized. Against that, experimental evidence suggests that the size of the infecting droplet cannot be large enough to carry more than a few bacilli and that multiple primary lesions are uncommon. These opposite factors have not yet been reconciled. [This is an excellent paper.]

John Lorber

RESPIRATORY TUBERCULOSIS

258. Clinical Usefulness of Riboflavin-tagged Isoniazid for Self-medication in Tuberculous Patients

K. W. DEUSCHLE, C. JORDAHL, and G. L. HOBBY. *American Review of Respiratory Diseases* [Amer. Rev. resp. Dis.] 82, 1-10, July, 1960. 7 figs., 4 refs.

While isoniazid can be detected in the urine only with difficulty, the drug may be tagged with riboflavin, a compound easily detected in urine. An investigation of the value of tagging isoniazid with riboflavin to confirm self-medication by tuberculous patients is reported in this paper from the New York Hospital-Cornell Medical Center and the U.S. Veterans Administration Hospital, East Orange, New Jersey. Patients received 5 to 10 mg. of isoniazid per kg. body weight in 50-mg. tablets, which also contained 8 mg. of riboflavin. The urinary excretion of riboflavin in these patients exceeded 2.5 μ g. per ml., ranging up to 100 μ g. per ml., compared with a maximum of 2.5 μ g. per ml. in patients not taking isoniazid and a maximum of less than 3.5 μ g. per ml. in those taking vitamin capsules. The authors consider that the use of riboflavin-tagged isoniazid constitutes a practicable method of determining whether self-medication is regularly carried out. I. Ansell

259. Chemotherapy in Resection for Pulmonary Tuberculosis. Problems of Extensive Disease and Drug-resistant Organisms

M. M. PYLE, H. T. LANGSTON, and K. H. PFUETZE. *American Review of Respiratory Diseases* [Amer. Rev. resp. Dis.] 82, 51-58, July, 1960. 6 refs.

The value of chemotherapy in patients subjected to resection for tuberculosis was studied in 358 patients operated on (extensive resection in 112) at the Chicago State Tuberculosis Sanatorium, Illinois. At the time of resection 100 patients had strains of tubercle bacilli which were resistant to 10 μ g. of streptomycin and 5 μ g. of isoniazid, and/or sputum positive for tubercle bacilli; most of these patients received viomycin, pyrazinamide,

or cycloserine. Surgical mortality was 1.7%, and tuberculous complications occurred in 5.4%. Follow-up examination in 340 patients after nearly 5 years revealed inactive disease in 88.2% and failure of treatment in 5%. Tuberculous complications occurred in 16 (16%) of 97 patients presenting a chemotherapeutic problem compared with 3 (1.2%) of 255 without such problems. The authors consider that the degree of success in resection varies directly with the chemotherapeutic control of the disease. I. Ansell

260. The Initiation of Chemotherapy in Pulmonary Tuberculosis in West Africans. Hospital and Ambulant Treatment Compared Using Streptomycyclidine-Isonicotinic Acid Hydrazide

W. J. BELL. *British Journal of Diseases of the Chest* [Brit. J. Dis. Chest] 54, 247-254, July, 1960. 15 refs.

A controlled study undertaken to determine the value of an initial short stay in hospital for patients given chemotherapy for tuberculosis is reported in this paper from the West African Council for Medical Research, Accra, Ghana. A total of 89 indigenous West African males, aged 15 to 40 years, with tuberculosis involving more than one lung zone (which was believed to be of recent origin and previously untreated), who were excreting tubercle bacilli sensitive to streptomycin and isoniazid, were allocated at random to a group given treatment in hospital (33) or to a group treated on an out-patient basis (56). The groups were closely comparable as regards clinical condition, bacteriology of the sputum, and the radiological appearances in the lungs. All were given an injection of "streptohydrazid", equivalent to 1 g. of streptomycin and 236 mg. of isoniazid, daily. Out-patients reported each day for injections but otherwise continued normal activities, including work, if desired, and normal diet. In-patients stayed in hospital for 12 weeks, but were allowed up for toilet purposes and to sit up for one hour daily; they received the standard hospital diet. The two groups received similar treatment for any incidental disease.

After 3 months no significant difference was observed between the two groups in respect of rate of clinical improvement, weight gain, or sputum conversion.

Janet Q. Ballantine

261. Surgical Treatment for Pulmonary Tuberculosis in Childhood

H. C. NOHL and S. J. STEEL. *British Journal of Diseases of the Chest* [Brit. J. Dis. Chest] 54, 255-264, July, 1960. 16 refs.

Between 1949 and 1958 inclusive 3,107 children under 16 years of age were treated for pulmonary tuberculosis at High Wood Hospital for Children, Brentwood. Of these, 71 (primary tuberculosis or its complications in 18, and chronic pulmonary tuberculosis in 53) underwent operation at the London Chest Hospital and these were selected for special study. The authors state that only a few children were treated surgically in the earlier years of the period under review and that a more accurate estimate of the proportion so treated is obtained by analysis of the figures during the second half of the

decade when 17 (3.3%) of 515 children with primary tuberculosis and 45 (14.6%) of the 309 with chronic lesions were subjected to surgery.

The indications for operation in the entire 71 cases were as follows. Of the 18 children with primary tuberculosis 2 had a large cavitated primary focus, 6 had obstructive emphysema causing persistent symptoms, 9 had persistent collapse and bronchiectasis, and one had emphysema. In the children with chronic tuberculosis the indications were similar to those which govern surgery in adults. No child was operated on for prophylactic reasons, and all those selected had symptoms due to the various complications of primary tuberculosis. All except 2 had chemotherapy, averaging 44 weeks in primary and 97 weeks in chronic cases. In the majority there was bacteriological or histological evidence of tuberculous activity at operation. Segmental lesions were more often the result of parenchymatous disease than of collapse. Bronchial obstruction due to pressure or ulceration from adenitis was not relieved by bronchoscopy, and it was found that incision of the capsule and evacuation of the abscess with closure of the bronchial defect was more satisfactory than any attempt at adenectomy, although if the subcarinal and para-oesophageal lymph nodes were involved adenectomy was carried out alone or in conjunction with resection of diseased lung parenchyma. Sleeve resections of bronchi were performed if healthy lung tissue remained distal to a stenosis.

Resection was the operation most often performed for parenchymatous disease, although in a boy of 14 years a 6-rib thoracoplasty arrested the disease and did not result in deformity. Extrapleural pneumothorax was abandoned because of the high rate of complications, but with all other procedures complications were rare. There were no deaths, and compared with adults the children made surprisingly good progress after operation and the results radiologically were good.

Janet Q. Ballantine

262. The Long-term Results of Resection in Children with Pulmonary Tuberculosis. (Résultats éloignés des exérèses pulmonaires chez l'enfant tuberculeux)

LOWYS, MANÉVY, JOLY, and TOBÉ. *Revue de Tuberculose et de Pneumologie* [Rev. Tuberc. (Paris)] 24, 648-667, May-June [received Aug.], 1960. Bibliography.

The authors review their experience at the Sanatorium du Roc-des-Fiz, Passy, Haute-Savoie, where between 1953 and 1958 they have performed pulmonary resections on 81 tuberculous children. Follow-up observations of between one and 6 years are reported. Most of the resected lesions were of the adult type, the remainder being cases of post-primary bronchiectasis or broncho-stenosis. Early in the series 5 patients in whom a lung had been destroyed by the disease were subjected to pneumonectomy, which was followed by a good subsequent clinical course. Lobectomy, rather than more limited resections, was carried out more often than would be the case in a similar series of adult patients, in the belief that the lung tissue of children expands easily and may even regenerate. There was no operative mortality and no serious postoperative complication other than

one case of chylothorax and one of pneumothorax, both of which responded to treatment. Late results have been excellent, with no mortality and no spread of disease, and all the patients are leading a life normal for their age.

Postoperative studies of respiratory function have been carried out in 41 cases and by and large showed that children readily adapt themselves satisfactorily to lung resection without serious disability. The radiological appearances in most cases eventually demonstrated only such minor changes as slight pleural thickening, although 6 patients retained considerable limitation of diaphragmatic movement. The authors paid great attention to the pre- and post-operative care of these children and stress the importance of bed rest and chemotherapy, both before and after operation. All operations were performed by the same surgical team and at all times there was close and continuous collaboration with and between the clinicians concerned in the management of the cases.

A. M. Macarthur

263. Cavitating Primary Pulmonary Tuberculosis in Infancy

N. JOFFE. *British Journal of Radiology* [Brit. J. Radiol.] 33, 430-439, July, 1960. 11 figs., 18 refs.

This paper discusses the way in which Bantu children, under 2 years of age, responded to a primary tuberculous infection, and is particularly concerned with the radiological findings in a series of 27 African children seen at Baragwanath Hospital, Johannesburg. All of these children were shown to have developed a primary cavity in the lung. Although the lesions were widely distributed there was a tendency for them to appear most frequently in the right upper lobe (9 cases), the right middle lobe (8 cases), and the left upper lobe (5 cases). The author stresses the diagnostic importance of small areas of consolidation associated with cavitation. In most cases the clinical examination of the patient had revealed crepitations and bronchial breathing, but the presence of a cavity was not suspected until radiological examination was carried out.

The methods by which cavitation can develop in the lung following a primary tuberculous infection are discussed. It is concluded that, as references in the literature to the development of cavitation in European children are rare, the prognosis after primary tuberculous infection is different in Bantu children, in whom bronchopneumonic tuberculous lesions frequently progress to cavitation.

[If the literature of some years ago is consulted, reference to cavitation in the lung is not really as infrequent as the author implies. The paper itself deals primarily with radiological appearances, and presents the details of systemic clinical investigations in only 3 patients. Most of the statements made appear in any standard textbook on pulmonary tuberculosis except, perhaps, the finding that destructive local progression of primary disease occurs more often in the African child than in the European child. This is a point of interest when it is recalled that Ghon observed, in his original series, 57 cases of cavitation in 169 children with primary pulmonary tuberculosis.]

W. Raymond Parkes

Tropical Medicine

264. Observations on Dehydration and Sweating

C. S. LEITHEAD and M. A. PALLISTER. *Lancet* [Lancet] 2, 114-117, July 16, 1960. 2 figs., 29 refs.

The authors of this paper from the Liverpool School of Tropical Medicine discuss the incidental finding of voluntary dehydration and reduced sweat rates in personnel of the Royal Air Force during acclimatization to the heat of Bahrain in the summer of 1959. The average 24-hour output of urine by these subjects before they left the United Kingdom was 1,070 ml., whereas in Bahrain the average of 168 such specimens was 567 ml. Of the 24-hour specimens collected in Bahrain 48% were under 500 ml. and 10% were 300 ml. or less, the specific gravity of the smaller quantities being correspondingly high.

The environmental temperatures were approximately 94° F. (34.4° C.) dry-bulb and 80° F. (26.6° C.) wet-bulb. The subjects, who remained well, were weighed daily. When the body weight was below average the subjects passed less urine and on changing from the lying to the standing position the pulse rate was faster and the pulse pressure smaller than when weight was above average. The secretion of both urine and sweat fell as body weight decreased and it was assumed that this was a result of dehydration. Thermal sweating was progressively reduced by dehydration, and response of the sweat glands to changes in body salt content simulated the response of the kidneys, which regulate salt concentration in the body by altering their own rate of water removal.

R. R. Willcox

265. Anhidrosis following Intravenous Bacterial Pyrogen

R. G. BANNISTER. *Lancet* [Lancet] 2, 118-122, July 16, 1960. 3 figs., 21 refs.

A study is reported from the National Hospital, Queen Square, London, of the effect upon the sweat rate of intravenous injections of a purified bacterial polysaccharide obtained from *Salmonella abortus equi* in 4 volunteers who were exposed to an artificial hot, humid climate such as exists in Aden. In all 4 subjects there was a complete cessation of sweating, which lasted 7 to 60 minutes, between 55 and 105 minutes after injection of the pyrogen. On all occasions on which the cessation of sweating lasted long enough for the injection to be given and sweat impressions to be taken, the sweat glands were stimulated to activity by an intracutaneous injection of methacholine chloride.

An attempt was made to imitate the syndrome of acute anhidrotic heat exhaustion by giving a dose of pyrogen which reduced sweating without causing a rigor. In 3 experiments 2 injections of small doses of pyrogen were given at an interval of 90 minutes. Neither dose by itself would have been expected to have had more than a trivial effect on body temperature, but on each occasion the double injection produced exaggerated febrile and anhidrotic responses. Although in the double-injection experiments a mild headache and fatigue were the only

symptoms at the moment of cessation of sweating, other symptoms were subsequently noted. Nausea was marked and in one case was accompanied by a feeling of chill, a cessation of sweating for 45 minutes, and a transient fall in oral temperature with a fall in blood pressure to 90/75 mm. Hg.

The rise in body temperature caused by the same doses of pyrogen in one subject was similar at 2 environmental temperatures which differed by 20° F. (11° C.), although an additional effector mechanism (shivering) was evoked at the lower temperature. This, the author considers, implies the presence of some kind of thermoreceptor cells relaying information about either the environmental temperature or the rate of rise in body temperature, or both, resulting in a modification of the temperature-regulating mechanisms appropriate to the particular environment.

R. R. Willcox

266. Use of Quinocide in Treatment and Prophylaxis of Vivax Malaria

A. Y. LYSENKO. *Bulletin of the World Health Organization* [Bull. Wld Hlth Org.] 22, 641-662, 1960. 26 refs.

Quinocide is a derivative of 8-aminoquinoline which differs from primaquine in the position of attachment of the methyl group in the side-chain, but has an antimalarial activity similar to that of primaquine. It was synthesized in the U.S.S.R. in 1952 [and in the U.S.A. in 1949] and has now taken the place of the more toxic 8-aminoquinoline compound plasmodium in the treatment in Russia of malaria due to *Plasmodium vivax*. It was introduced when malaria as a mass disease had been eliminated in the U.S.S.R. by insecticides and drugs then available. Quinocide is now being used for the eradication of residual foci of epidemic malaria and for dealing with recrudescences in cleared areas.

The author reviews the laboratory investigations in animals and human volunteers in which quinocide was shown to be rapidly absorbed from the gut and not to accumulate in the tissues. It was generally well tolerated and side-effects (abdominal discomfort, slight cyanosis, and drug fever) were infrequent and transient. Haemolysis occurred more often in healthy persons than in patients with malarial fever. There was some evidence that the drug might cause renal irritation. When proguanil, pyrimethamine, or chloroquine was administered at the same time as quinocide the side-effects were more pronounced. The author states that quinocide is given in a dosage of 15 mg. daily for 14 days or 23 mg. daily for 10 days. It acts on tissue forms of the malaria parasite and is given after courses of treatment with mepacrine or proguanil for the radical cure of *P. vivax* infections. In epidemic foci pyrimethamine or proguanil is administered during the transmission season to suppress malarial fever and kill early tissue parasites; during the inter-epidemic season a course of quinocide is given to kill the persisting tissue forms.

[Quinocide, under the code number CN1115, was rejected by American workers in favour of primaquine because tests in animals showed the latter to be less toxic. A recent trial in non-immune volunteers (see *Abstr. Wld Med.*, 1961, 29, 14, Abstract 43) has shown that the haemolytic action of quinocide is greater and its curative effect less than those of primaquine. No comparison with primaquine is reported in the present paper. Quinocide is, however, a great improvement on plasmocide (which has neurotoxic properties) and its systematic use in the eradication of residual malaria in the U.S.S.R. is admirable.]

L. G. Goodwin

267. Malaria in the Pare Area of Tanganyika. Part II. Effects of Three Years' Spraying of Huts with Dieldrin
C. C. DRAPER and A. SMITH. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 54, 342-357, July, 1960. 13 refs.

The authors of this paper from the East African Institute of Malaria describe the effects on the vector mosquito and on the incidence of malaria in human beings of spraying 1,500 huts with a water-dispersible preparation of dieldrin, giving an approximate wall dosage of 80 mg. per square foot (900 mg. per square metre) for the first and 40 mg. per square foot for subsequent applications. The spraying was carried out at intervals of 8 months over a period of 3 years. Inside walls, roofs, and ceilings in about 90% of the habitations in the district were sprayed.

Anopheles funestus had apparently disappeared 7 months after the first spraying. The number of *Anopheles gambiae* was reduced in the roadside villages, but not in the swampy areas where the mosquito fed readily on cattle and had outside resting places. No evidence was found of this mosquito becoming resistant to dieldrin, but resistance was detected in *Culex fatigans*, *Pulex irritans*, and *Pediculus corporis*. Mosquitoes were irritated on entering a freshly-sprayed hut and often left before biting. Mortality among the mosquitoes was high and there was a considerable fall in all human malaria indices, but evidence from several sources indicated that a "low degree of malaria transmission" continued throughout; possible reasons for this are discussed.

Clement C. Chesterman

268. Nitrofurazone in the Treatment of Sleeping Sickness Due to *Trypanosoma rhodesiense*
F. I. C. APTE. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 54, 225-228, May, 1960. 7 refs.

The results obtained with nitrofurazone in the treatment of 9 patients with sleeping sickness in whom the organisms were resistant to melarsen oxide combined with BAL ("Mel B") are reported in this paper from the Medical Department, Tanganyika. The drug was given by mouth in 3 or 4 divided doses up to a total of 2 g. a day, generally for 5 to 7 days, and then, after a rest period of one week, the course was repeated. Some patients received a third and even a fourth course, the total dosage varying between 170 mg. and 583 mg. per kg. body weight. The condition of all 9 patients before

treatment started was considered to be "hopeless", but 4 responded well to nitrofurazone, and were alive and well 1 to 2 years after treatment. A relapse occurred in one patient after nitrofurazone alone, but the infection responded to a further course supplemented with Mel B; however, the prognosis in this last case was considered to be doubtful.

No toxic effects were seen in any of the patients who responded favourably. In the 4 patients in whom treatment failed peripheral neuritis developed to some degree and in 2 of them it was incapacitating. It is pointed out that the effect of nitrofurazone on the seminiferous tubules should be borne in mind during administration, although this drug would ordinarily be given only when others have failed and when the saving of life is the immediate concern.

I. M. Rollo

269. Cultivation of the African Sleeping Sickness Trypanosomes from the Blood and Cerebrospinal Fluid of Patients and Suspects

D. WEINMAN. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 54, 180-190, March [received June], 1960. 26 refs.

A new method of culturing *Trypanosoma gambiense* and *T. rhodesiense* from samples of human blood and cerebrospinal fluid (C.S.F.) is described in this paper from the Department of Microbiology, Yale University School of Medicine, New Haven, Connecticut. The medium consists of an autoclaved nutrient-agar base and citrated human blood, the plasma from which is separated off and inactivated at 56° C. and the erythrocytes washed in saline. Polyvinyl sulphuric acid is used as the anticoagulant for donor blood because of its high anti-complementary activity. The cultures, which usually become positive in 5 to 30 days after inoculation with 1.8 ml. blood and 0.2 ml. of anticoagulant solution, provide an abundance of trypanosomes.

Specimens of blood and C.S.F. from 34 patients known to have trypanosomiasis were cultured; in 27 instances cultures were positive, but in the remaining 7 the cultures were found to be contaminated with either bacteria or fungi and no trypanosomes were present. This was consistent with a previous observation that the presence of bacteria or fungi almost invariably inhibits multiplication of trypanosomes.

Blood and C.S.F. from 22 suspects who had been declared negative after conventional examination were also cultured. Infection was proved by culture in 5. one of whom had previously been treated with pentamidine and trypanamide. In many of the remaining 17 the cultures were contaminated and probably would not have grown trypanosomes even if the organisms had been present.

No difference was observed whether the organism was *T. gambiense* or *T. rhodesiense* and no difficulty was experienced in cultivating trypanosomes from the C.S.F. The author considers that control of contamination can probably be attained by improved technique and the use of suitable antibacterial and antifungal substances.

I. M. Rollo

Nutrition and Metabolism

270. Vitamin A and Vitamin E in Human Blood. I. Levels of Vitamin A and Carotenoids in British Men and Women, 1948-57

Z. A. LEITNER, T. MOORE, and I. M. SHARMAN. *British Journal of Nutrition [Brit. J. Nutr.]* 14, 157-169, 1960. 10 figs., 30 refs.

Vitamin A and total carotenoids were estimated during the decade 1948-57 in the blood serum of more than 700 British men and 500 women in whom no serious disease could be detected. Wide individual variations were found in both sexes. The mean values for equal numbers of each sex were 158 i.u. vitamin A and 126 μ g. carotenoids per 100 ml. serum. In groups of men, whether arranged according to age, seasonal or biennial period, mean values for vitamin A were always about 20% higher than for women. For carotenoids the relationship was reversed, with mean values about 8% higher for women than for men. The difference between men and women in the values for vitamin A tended to widen with increasing carotenoid levels. In men mean values for vitamin A increased with age until a maximum was reached in the age group 50 to 59 years. In women also vitamin A increased with age until at 70 to 79 years the usual sex difference had disappeared. Mean carotenoid values in men ran almost parallel with vitamin A, but in women unexpectedly high values were found under the age of 30 years.

In both sexes higher mean values for carotenoids were found in spring and summer than in autumn and winter. In women, vitamin A varied little at the different seasons, but in men the mean values in summer and autumn were slightly higher than in winter and spring. In both sexes blood vitamin A appears to have increased since the removal of wartime food restrictions. The increases appear to have run roughly parallel with increases in the intake of vitamin A as estimated in the National Food Survey. Increases in blood carotenoids over the same period were less pronounced.

It seems probable that the sex differences in the levels of vitamin A and carotenoids may be due, at least in part, to greater efficiency in the conversion of carotene into vitamin A by men than by women.—[Authors' summary.]

271. Effect of Physical Exercise on Alimentary Lipaemia

H. COHEN and C. GOLDBERG. *British Medical Journal [Brit. med. J.]* 2, 509-511, Aug. 13, 1960. 2 figs., 11 refs.

A study is reported of the effect of exercise on the clearing of alimentary lipaemia in 22 healthy medical students (12 male and 10 female) aged 20 to 25 years. Initially, 6 of the students received a 75-g. fatty breakfast, after which 3 of them rested and 3 exercised by walking 6 miles. Blood samples were taken into oxalated tubes before breakfast and at intervals of 3, 5, and 7 hours after the meal. In each case the plasma turbidity was determined spectrophotometrically at

6,700 Å. After 10 days the study was repeated, but on this occasion the 3 students who had previously rested took exercise and those who had taken exercise rested. A second group of 14 students was studied after they had consumed a 60-g. fatty breakfast. The method adopted was the same as that in the first group of 6 students except that only one blood sample was taken 6 hours after eating. The 2 remaining students received a 75-g. fatty breakfast and then took their exercise in the form of cycling on a stationary machine for two periods of half-an-hour each, the cycling in each period being equivalent to 5 miles (8 km.) up a slight incline.

It was found that in a statistically significant number of cases (the *t* test being used) the plasma turbidity was less after exercise than after rest.

B. M. Ansell

272. The Storage of Vitamin D in the Body. (К вопросу о депонировании витамина D в организме)

A. M. НВУЛ'. *Педиатрия [Pediatrija]* 38, 33-37, Sept., 1960. 34 refs.

Vitamin-D deficiency affects primarily the central nervous system, but it also influences phosphorus-calcium metabolism. The method of introducing vitamin D into the body is still debatable. Stoss therapy, whereby massive doses are administered within 2 or 3 days, has been discarded by all who have tried it, since the vitamin is poorly absorbed by the body. However, in view of the duration of its effect it must be assumed that vitamin D is stored in the body. Further to the work of Cruickshank and Kodicek (*Biochem. J.*, 1954, 58, 172) who experimented on rats but observed absorption of the vitamin for only a short period (24 and 48 hours), the present author has extended these experiments by observing for 25 days rats which were given a rachitogenic diet and, in the case of two groups, supplements of vitamin D. Group 1 received 14,700 i.u. in 3 days, Group 2 the same amount in 21 days (that is, 700 i.u. per day), while a control group received no vitamin. The mean results of 8 to 10 experiments for each group are shown in the following table.

Tissue	Content of Vitamin D ₂ (in I.U.) in 1 g. of Tissue		
	Group 1	Group 2	Control Group
Liver	450	350	nil
Skin	400	280	nil
Intestine ..	20	20	nil
Muscles ..	15	15	nil

The author concludes that the storage of vitamin D in the tissues is definite, and is irrespective of whether it is administered in massive or in fractional doses (over 21 days). He recommends massive doses in cases of acute hypovitaminosis-D.

H. W. Swann

Gastroenterology

273. Aspirin, Gastrointestinal Bleeding, and Peptic Ulcer

M. LEVRAT and R. LAMBERT. *American Journal of Digestive Diseases* [Amer. J. dig. Dis.] 5, 623-631, July, 1960. 22 refs.

Severe gastro-intestinal symptoms following the oral ingestion of aspirin developed in 52 patients under treatment at the Hôpital Edouard-Herriot, Lyons, during 1957 and 1958. The interval between the last dose of aspirin and the occurrence of symptoms was less than 24 hours. Gastro-intestinal haemorrhage occurred in 39 of the patients; in 15 of these an active ulcer was demonstrated on x-ray examination, but in 21 the radiological findings were negative and the haemorrhage could not be related to a definite lesion; 3 patients in this group had alcoholic cirrhosis of the liver. In the remaining 13 patients in the series no haemorrhage occurred, but x-ray examination revealed an active ulcer. Thus, the presence of active peptic ulcer was radiologically proven in 28 cases. Moreover, in 11 patients in whom the radiological findings were negative there was evidence of what the authors term an "ulcerous predisposition"—that is, a previous healed peptic ulcer and/or a direct family history of peptic ulcer. When these were taken into consideration the number of patients with an ulcerous predisposition became 39, or 75% of the total.

The pathogenesis is discussed. The authors conclude that the mechanism is mainly that of a local irritant action of the drug on the gastric mucosa, and that this action may have "serious effects in persons of a special constitution".

Joseph Parness

STOMACH AND DUODENUM

274. An Evaluation of the Einhorn String Test

J. A. EWART, H. N. STURTEVANT, and B. H. SULLIVAN JR. *American Journal of Digestive Diseases* [Amer. J. dig. Dis.] 5, 632-638, July, 1960. 2 figs., 8 refs.

Before the introduction of radiology for diagnosis of diseases of the gastro-intestinal tract, the Einhorn string test was an accepted diagnostic procedure for peptic ulcer. In the test, as described by Einhorn in 1909, the patient swallowed a measured thread of braided silk, weighted at the distal end, which was left in the upper gastro-intestinal tract overnight and removed the next morning. The string was then inspected for a blood stain, and it was thought that the distance of the stain from the incisor teeth would indicate the site of the ulcer. Two separate groups of workers in the U.S.A., in 1949 and 1952 respectively, modified the string test, using a soft cotton string instead of silk or linen. One group found that 72.3% of the results of the string test (out of 114 tests in 100 patients) agreed with those of x-ray examination, while the other group reported that the

string test was accurately diagnostic in 81% of a group of 98 cases.

In the present paper a further evaluation of the string test is reported, the test being carried out in 25 unselected patients at the Brooke Army Hospital, Fort Sam Houston, Texas. All the patients were subjected to at least one x-ray examination of the upper gastro-intestinal tract. The diagnoses established or later confirmed at operation included duodenal ulcer in 16 cases and gastric ulcer in one. The string test was used in the same way as that described by Einhorn, but with the following modification: radio-opaque markers were placed at 5-cm. intervals from the distal end of the string, and before the string was removed the following morning the patient was given a thin solution of barium by mouth and the markers thus located radiologically with reference to the stomach and duodenum.

There were no blood stains on the string in the duodenal region in the 16 cases of duodenal ulcer; in 9 of these cases the blood stain was in the region of the oesophago-gastric junction and in 4 cases it was along the lesser curvature of the stomach or in the antral region. In the case of gastric ulcer no blood stain was noted at the site of the ulcer in the antral region, but a stain was present at the oesophago-gastric junction. The blood stain was along the lesser curvature of the stomach in one patient with achalasia. A patient with gastritis was the only one in the series to show a blood stain in the duodenal region. Blood staining of the string was also found in cases of bronchiectasis, sickle-cell anaemia, and cholelithiasis.

The authors conclude that the string test is of no practical value in the diagnosis or location of peptic ulcer.

Joseph Parness

275. Gastric Lesions, Including Exfoliative Cytology: a Diagnostic Approach

W. T. ARNOLD, J. HAMPTON, W. OLIN, H. GLASS, and C. CARRUTH. *Journal of the American Medical Association* [J. Amer. med. Ass.] 173, 1117-1120, July 9, 1960. 4 figs., 2 refs.

Of 300 patients with upper gastro-intestinal pain examined at the Herman Hospital, Houston, Texas, 18 had carcinoma of the stomach. Cytological examination proved to be the most accurate diagnostic procedure, the technique being as follows. A 16 F. Levin tube was passed a distance of 60 cm. and the fasting contents of the stomach were aspirated. A lavage solution containing 500 ml. of an acetate buffer (pH 5.6) with added chymotrypsin (7 mg.) was then instilled into the stomach, left there for 10 minutes, then aspirated and slides prepared, stained by the Papanicolaou technique, and examined microscopically. In 13 of the 18 cases the cytological findings were diagnostic of carcinoma. False positive results were obtained in only 2 of the total series of 300 cases.

The authors emphasize the importance of considering the radiological and gastroscopical findings in conjunction with the results of cytological examination. In the total series of cases erroneous diagnoses were suggested after cytological examination in 7 cases, after x-ray examination in 22, and after gastroscopy in 14, but when the over-all picture was studied only 3 cases were inaccurately diagnosed.

[With such a small total number of cases of cancer in the series undue importance should clearly not be attached to these figures.]

Guy Blackburn

276. Activation of Peptic Ulcer by Nicotinic Acid. Report of Five Cases

W. B. PARSONS JR. *Journal of the American Medical Association [J. Amer. med. Ass.]* 173, 1466-1470, July 30, 1960. 11 refs.

The activation of peptic ulcer by nicotinic acid is discussed with reference to the findings in 5 patients at Jackson Clinic, Madison, Wisconsin, who were given high doses of the drug in an attempt to reduce hypercholesterolaemia. There was evidence of aggravation of ulceration in all 5 patients, with occult bleeding in one patient. The dyspeptic symptoms were controlled by using a buffered preparation of nicotinic acid in place of the acid itself. [The buffer used is not specified.]

D. A. K. Black

277. Stilboestrol, Phenobarbitone, and Diet in Chronic Duodenal Ulcer: a Factorial Therapeutic Trial

S. C. TRUELOVE. *British Medical Journal [Brit. med. J.]* 2, 559-566, Aug. 20, 1960. 3 figs., 32 refs.

The much higher incidence of duodenal ulcer in males than in females has given rise to many suggestions concerning the influence of sex hormones upon ulcer formation. About 1940 oestrogen therapy was tried by a number of workers, on the supposition that circulating oestrogens might exert some inhibitory effect upon peptic ulcer. The present study, reported from the Radcliffe Infirmary, Oxford, was designed to test the effect of small doses of stilboestrol on the course of uncomplicated duodenal ulcer in males. A group of 80 patients were chosen and 3 agents, stilboestrol, phenobarbitone, and a "gastric diet", were tested in a factorial experiment, "blocks" of 8 patients being given real and dummy tablets of phenobarbitone and stilboestrol. All the subjects had positive x-ray evidence of duodenal ulcer and a typical history of at least one year's duration. The trial period was 6 months, during which 0.5 mg. of stilboestrol twice daily, or phenobarbitone 1 grain (65 mg.) twice daily, was given. The trial was carried out between 1952 and 1954, and the author reviews the results both of the short-term findings at the end of the treatment (6 months) and the long-term findings at the end of 5 years. The clinical condition and the radiological findings were used to assess the results.

The short-term results showed that in those taking stilboestrol, freedom from severe symptoms was almost universal during the trial period, and the ulcer crater disappeared in 24 patients. Neither phenobarbitone nor a gastric diet influenced the liability to exacerbation

of symptoms; there was, in fact, no indication that either of these agents significantly affected either the short- or the long-term course of the disease. Stilboestrol, on the contrary, appeared to produce clinical and radiological "cure" more than twice as often as in the controls, and surgery was needed in only one-third of these patients as compared with controls.

The author [rightly] points out that this method of treatment is still experimental and draws attention to the side-effects of stilboestrol, which, in the doses given, consisted in loss of sexual potency and gynaecomastia, although both these disappeared on cessation of treatment. It is uncertain how long administration of stilboestrol should be kept up, or whether some non-feminizing hormone might produce similar effects.

[It seems likely from these studies that with further work, especially in patients with a short history of duodenal ulcer, useful developments may be expected. It is certainly clear that standard ulcer diets have little effect upon the natural course of the disease, and this study will help to draw attention again to the lack of exact knowledge of the aetiology of ulcer. No mention is made of acid secretion in the patients studied or of the effects of stilboestrol upon gastric secretion or gastric motility.]

Thomas Hunt

278. The Etiology and Management of the Dumping Syndrome following a Gastroenterostomy or Subtotal Gastrectomy

W. E. ABBOTT, H. KRIEGER, S. LEVEY, and J. BRADSHAW. *Gastroenterology [Gastroenterology]* 39, 12-27, July, 1960. 6 figs., 34 refs.

The factors involved in the production of early post-cibal symptoms after gastric surgery are discussed in this paper from the Western Reserve University School of Medicine, Cleveland, Ohio. It is emphasized that assessment of the results of operation from the patient's replies to a questionnaire or at an interview is unsatisfactory and that only by observing the patient in hospital can the success or degree of failure of surgery be adequately judged. The authors then describe their method of evaluating gastro-intestinal function in such patients, which consisted first in x-ray examination following ingestion of a mixture containing 70 g. of barium blended with milk, ice-cream, sugar, and a proprietary protein preparation. Radiographs taken in the upright position at intervals of 1, 20, 45, and 90 minutes after the meal showed the rate of emptying of the stomach and also the degree of intestinal hurry. The findings were then correlated with the objective and subjective symptoms of the individual patient and served as a basis for comparison if further surgery was performed. The authors also attempted to determine whether excessive amounts of serotonin were liberated into the intestine in patients with the dumping syndrome, but the results were inconclusive. They consider that the most important factor in preventing or curing dumping is the preservation of the function of the stomach as a reservoir and they advocate the use of small stomata.

[This is a comprehensive paper which should be read in full by those interested.]

B. F. Swynnerton

LIVER AND GALL-BLADDER

279. Contribution of Cineradiography to Study of the Function of the Human Biliary Tract

J. CAROLI, P. PORCHER, G. PÉQUIGNOT, and M. DELATTRE. *American Journal of Digestive Diseases* [Amer. J. dig. Dis.] 5, 677-696, Aug., 1960. 23 figs., 18 refs.

Since 1939 the authors have studied the human biliary tract during or after surgical intervention, using a combination of cineradiography, cholangiography, and manometry, and in this paper from the Hôpital Saint-Antoine, Paris, they describe the findings obtained by this technique in 34 patients.

They demonstrated that at the basic residual pressure in the common duct of 12 to 18 cm. of water the rhythm of the sphincter of Oddi is about 3 seconds open and 3 seconds closed, and that elevation of pressure slows the rhythm to about 6 seconds open and 4 seconds closed. Atropine leaves the over-all rhythm unchanged while increasing the open phase at the expense of the closed; at the same time it abolishes the effect on rhythm of changes of pressure. At any given pressure, atropine, together with other relaxants such as amyl nitrite, or a fatty meal increases perfusion flow, whereas morphine has an opposite and more spectacular effect. A perfusion pressure of 35 cm. is necessary before the sphincter opens, the open phase is shortened, and the closed phase prolonged. The sphincter of Oddi can have a rhythm which is completely independent of the surrounding duodenal muscle. [The authors' further observations on reflux into the pancreatic ducts are not suitable for abstracting.]

[This paper, which is based on a study with what is possibly the best image intensifier and cinefilm apparatus available, should be read in the original. Since 31 of the 34 patients had lithiasis, in 27 cholecystectomy was performed, and in 12 the common duct was explored for stones, some of the sphincters of Oddi were admittedly abnormal, so that the measurements of rhythm are presumably based on selected cases. This limitation (a serious one to British-trained scientists) is not discussed.]

Denys Jennings

280. Shunt Encephalomyelopathy. I. Recurrent Protein Encephalopathy with Response to Arginine

L. ZIEVE, D. F. MENDELSON, and M. GOEPFERT. *Annals of Internal Medicine* [Ann. intern. Med.] 53, 33-52, July, 1960. 3 figs., 8 refs.

The authors describe in detail 3 cases of encephalomyelopathy following portacaval anastomosis seen at the Veterans Administration Hospital, Minneapolis, Minnesota. The first 2 patients had undergone both gastrectomy and a portacaval anastomosis before they showed any neurological abnormality. The third patient had been subjected to an extensive resection for carcinoma of the pancreas in which the portal vein was divided and the superior mesenteric vein anastomosed to the inferior vena cava. The first 2 patients had well-marked portal cirrhosis but the third showed evidence of a mild biliary cirrhosis only. All 3 patients showed extreme sensitivity and a steadily declining tolerance to protein. The

development of paraplegia in 2 seemed to be related to episodes of coma.

The authors state that they have given arginine, either the glutamate or the hydrochloride, in some 40 cases of hepatic coma and obtained a number of unequivocal responses, but in none was the response so sensitive or so prompt as in the 3 cases now described. The amount of arginine needed to restore the mental state of the patient to normal was directly proportional to the severity of the coma. In mild cases 25 g. intravenously was sometimes sufficient, but the usual minimum dose was 50 g., and 100 g. was often required. An interval of 12 to 24 hours usually elapsed between administration of the drug and improvement in the mental state. There was no difference in efficacy between the glutamate and the hydrochloride.

It is suggested that inadequate dosage of 50 g. or less may be the reason why others have not found this treatment to be successful.

T. D. Kellock

281. Shunt Encephalomyelopathy. II. Occurrence of Permanent Myelopathy

L. ZIEVE, D. F. MENDELSON, and M. GOEPFERT. *Annals of Internal Medicine* [Ann. intern. Med.] 53, 53-63, July, 1960. 2 figs., 12 refs.

The neurological changes seen at necropsy on one of the 2 cases (see Abstract 280) in which spastic paraplegia developed in the course of persistent and recurrent portal-systemic encephalopathy are described. The most consistent general finding was widespread proliferation of Alzheimer's Type-II glial cells. There was an area of spongy degeneration in the putamen and a selective demyelination of the pyramidal tracts. This last occurred maximally in the lower spinal cord and gradually decreased higher up, there being no abnormality of the tracts higher than the cervical region and no demyelination in the medulla, pons, cerebral peduncles, or internal capsule. The authors review 3 reported cases in which the findings were similar. The possible aetiological factors are discussed, including the probable imbalance of amino-acids as suggested by the response to arginine.

T. D. Kellock

INTESTINES

282. Malabsorptive Syndrome Induced by Neomycin: Morphologic Alterations in the Jejunal Mucosa

E. D. JACOBSON, J. T. PRIOR, and W. W. FALOON. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 56, 245-250, Aug., 1960. 3 figs., 7 refs.

Neomycin when given by mouth may give rise to a malabsorption syndrome. The investigation herein reported was undertaken to determine whether treatment with neomycin is associated with histological changes in the jejunal mucosa, mucosal specimens obtained at the time of operation or by blind biopsy being examined. Changes similar to those observed in idiopathic steatorrhoea were noted in 11 out of 12 specimens from patients treated with neomycin, but in none from patients not so treated. They included clubbing of the

villi, oedema of the lamina propria, and an increase in the number of lymphocytes and plasma cells within the lamina propria, and appeared as early as 4 days after the start of neomycin therapy. In one instance serial biopsy specimens showed that the jejunal mucosa returned to normal 18 days after withdrawal of the drug. The findings suggest that the malabsorptive state induced by neomycin is related to the changes seen in the jejunal mucosa.

D. Geraint James

283. Ulcerative Colitis in Older Age Patients

Z. T. BERCOVITZ. *Gastroenterology* [Gastroenterology] 39, 28-33, July, 1960. 10 refs.

The clinical histories of 57 ulcerative colitis patients 50 years of age or older have been reviewed; 36 patients (63%) had the onset of disease after the age of 50. The clinical results in this group of 36 patients showed that one-third required emergency surgery and 7 of the 12 patients died postoperatively. Two others died while under medical management and 61% are in clinical remission. There is a pattern of increasingly grave prognosis as the age of onset rises. Of the 21 patients whose onset occurred when they were under 50 years of age 76% are in clinical remission and the only 2 deaths were due to carcinoma. Three patients received surgical treatment and are clinically well. Relapses occurred predominantly at the same season of the year as onset of the disease. Prolonged remissions of up to 19 years' duration have been observed, but in spite of freedom from symptoms there is progression of the disease in all cases, as shown by repeated x-ray studies of the bowel.—[Author's summary.]

284. Dilatation of the Colon, a Serious Complication of Ulcerative Colitis

B. I. KORELITZ and H. D. JANOWITZ. *Annals of Internal Medicine* [Ann. intern. Med.] 53, 153-163, July, 1960. 2 figs., 6 refs.

This is a review of 19 episodes of toxic dilatation of the colon in 16 patients who were being treated for ulcerative colitis at Mount Sinai Hospital, New York. All the patients were febrile, toxic, and dehydrated. The abdomen was often soft except in areas of acute tenderness, but perforation was suspected clinically in 9 patients and confirmed at operation in 4, although in 3 others who were subjected to laparotomy no perforation was found. The most typical radiological feature was the localization of the dilatation to colonic segments. Often deeply penetrating ulcers, which from previous barium enema examinations were known to be present, were seen in plain radiographs. The transverse colon was involved in all cases, possibly owing to trapping of gas between the 2 flexures and consequent distension and further destruction of the bowel wall. Of the 16 patients 3 died, and of 11 who were operated on 10 recovered, usually after a very long and stormy postoperative course. Nearly all the patients had received steroids, but the authors are undecided on the evidence available whether this treatment contributed in any way to the development of the complications. Similarly there was no evidence that hypopotassemia was a causative factor. The authors

advocate a decompressing caecostomy as an emergency measure, to be followed if necessary by colectomy.

T. D. Kellock

285. Auto-immune Reactions in the Course of Ulcerative Colitis

J. POLCAK and V. VOKURKA. *American Journal of Digestive Diseases* [Amer. J. dig. Dis.] 5, 395-405, May, 1960. 14 refs.

The authors, working at the University of Brno, Czechoslovakia, have studied the immunological reactions in the serum of 30 patients with ulcerative colitis and 175 suffering from various other conditions, the collodion agglutination technique with antigen derived from the mucosa and submucosa of the human colon being used. Appropriate control studies with normal serum and uncoated collodion particles were carried out.

In all the patients with ulcerative colitis there was a positive titre greater than 1:4, the highest titre being 1:64. In 4 selected patients—2 with ulcerative proctitis and 2 with ulcerative colitis—the serum agglutinated collodion particles coated with antigen derived from different parts of the large bowel, but none of these sera gave a positive reaction with antigen derived from the ileum, stomach, or other organs. All the control sera gave a negative reaction. Serial observations on 9 patients showed that a positive titre was reduced, and in one case disappeared, after total proctocolectomy. In medically treated patients clinical improvement was sometimes accompanied by a fall in the antibody titre.

The authors suggest that these antibodies arise from the alteration of a normal bowel component, perhaps by bacteria or their toxins, and that the finding of these antibodies favours the view that ulcerative colitis is an auto-immune disease.

G. L. Asherson

286. Some Notes on the Epidemiology of Nonspecific Ulcerative Colitis. An Apparent Increase in Incidence in Jews

H. A. WEINER and C. M. LEWIS. *American Journal of Digestive Diseases* [Amer. J. dig. Dis.] 5, 406-418, May, 1960. Bibliography.

The authors of this paper from the Veterans Administration Hospital, East Orange, New Jersey, summarize the literature on the incidence of ulcerative colitis among Jews, and then discuss their findings at two Veterans Administration Hospitals, which showed that the incidence was higher in Jewish than non-Jewish patients. At the first hospital in 1949-50 only 15% of all patients admitted were Jews, but 17 (57%) of the 30 patients with ulcerative colitis were Jews. The corresponding figures for Roman Catholics were 55% and 8 (27%). At the second hospital during the period 1952 to 1959 6% of the patients admitted and 13 (22.4%) of the 56 patients with ulcerative colitis were Jews. The figures for Roman Catholics were 50% and 28 (48%).

The authors consider that these figures support the view that ulcerative colitis is commoner among Jewish people, but that current knowledge is inadequate to determine whether the responsible factors are environmental or hereditary.

G. L. Asherson

Cardiovascular System

287. The Effect of Disodium EDTA on Digitalis Intoxication

J. L. ROSENBAUM, D. MASON, and M. J. SEVEN. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 240, 77-84, July, 1960. 9 figs., 14 refs.

The action of digitalis on the myocardium is potentiated by the presence of calcium ions and by potassium deficiency. Intracellular potassium levels are influenced by both calcium and digitalis and the lowering of plasma calcium ion levels appears to increase the intracellular potassium concentration. The treatment of digitalis poisoning with potassium may thus be dangerous and this paper describes the effect of lowering the serum calcium level with intravenous sodium calciumedetate (EDTA) in digitalis intoxication. The investigation was carried out at the Hahnemann Hospital, Philadelphia, where 6 patients with digitalis poisoning were treated with 3 g. of EDTA as a 1.2% solution in 5% aqueous glucose solution, given intravenously over 20 to 30 minutes. In 5 cases arrhythmia was controlled rapidly but in one nodal tachycardia persisted. It is noted that the effect of EDTA may be transient in some cases, but this treatment can be followed by oral potassium chloride and other measures. The toxic effects of EDTA were slight, only transient paraesthesiae, transient hypotension, and the occasional appearance of a positive Trousseau sign being seen.

It is concluded that EDTA should be the first line of treatment of dangerous digitalis-induced arrhythmias, especially if ventricular tachycardia is suspected.

David Phear

288. A Case of Subacute Rickettsial Endocarditis; with a Survey of Cardiac Patients for this Infection

B. P. MARMION, F. E. HIGGINS, J. B. BRIDGES, and A. T. EDWARDS. *British Medical Journal* [Brit. med. J.] 2, 1264-1267, Oct. 29, 1960. 1 fig., 9 refs.

289. Bacterial Endocarditis following Surgery for Congenital Heart Disease

L. M. LINDE and H. L. HEINS. *New England Journal of Medicine* [New Engl. J. Med.] 263, 65-69, July 14, 1960. 35 refs.

The authors of this paper from the University of California School of Medicine, Los Angeles, report the development of bacterial endocarditis in 7 out of 550 patients subjected to cardiac operations between July, 1955, and November, 1959, including 5 out of a group of 205 patients in whom the extracorporeal heart pump was used. The congenital heart lesions included ventricular septal defect in 3 cases (repair being carried out in 2 and cardiomy without repair in one); tetralogy of Fallot in 2 (repaired by using an "ivalon" patch); cyanotic pseudotruncus in one case (subjected to Blalock's operation); and patent ductus arteriosus in one

(treated by closure). The organisms responsible for the endocarditis, which were resistant to many of the common antibiotics, were *Staphylococcus aureus* (2 cases), *Achromobacter* species (2), *Pseudomonas aeruginosa* (1), *Neisseria pharyngis* (1), and *Micrococcus* species (1). The usual classic signs of subacute or even acute bacterial endocarditis were not striking. All the patients had high fever, but embolic manifestations, finger clubbing, and splenomegaly were absent. Blood cultures were positive in all. The course of the disease was rapid in the 2 patients who died.

It is concluded that altered host and site resistance increases sources of exposure and that infection with unusual bacteria results in a more rapidly progressive and malignant disease.

C. Bruce Perry

290. Coronary Artery Disease. [The Jephcott Lecture]

H. FLOREY. *British Medical Journal* [Brit. med. J.] 2, 1329-1335, Nov. 5, 1960. 1 fig., 46 refs.

291. Sublingual Erythrol Tetranitrate in the Treatment of Angina Pectoris. Effect of Varying the Dose and Rate of Administration

G. E. ALTMAN, J. E. F. RISEMAN, and S. KORETSKY. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 240, 66-76, July, 1960. 3 figs., 7 refs.

In a previous trial of various nitrites the authors showed (*Circulation*, 1958, 17, 22; *Abstr. Wld Med.*, 1958, 24, 167) that erythrol tetranitrite (E.T.N.) was more effective for prevention of angina pectoris when administered as buccal or sublingual tablets than when swallowed. A further trial of E.T.N. given by these methods is reported from the Beth Israel Hospital (Harvard and Tufts Medical Schools), Boston. The study included 14 patients with angina who were seen at weekly intervals when the frequency of angina, the ability to work, and the effect of performing a standard two-step test were recorded.

The time for disintegration of the E.T.N. tablets was on the average some 20 minutes less under the tongue than in the buccal cavity, compressed tablets taking from 20 to 30 minutes to disappear when held in the cheek.

It was found that patients who did not respond to nitroglycerin did not respond to E.T.N., even when the dose was increased to 60 mg. three times daily. In those who did respond, sublingual E.T.N. powder produced a maximum improvement in exercise performance after 1 to 2 hours, with some effect lasting for 3 to 4 hours. Prolonged benefit was obtained, both with tablets with slow disintegration and from those which broke up rapidly and with these a dose of 5 mg. was sometimes as effective as one of 15 mg. Among the side-effects noted were transient burning of the mouth, headache, dizziness, and occasional fainting, and there was often a moderate decrease in blood pressure.

David Phear

292. Treatment with Chlorothiazide of 480 Cases of Heart Failure. (Traitement par la chlorothiazide de 480 cas d'insuffisance cardiaque)

J. HIMBERT and J. LENÈGRE. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [Bull. Soc. méd. Hôp. Paris] 76, 781-796, June 10-17 [received Aug.], 1960. 4 figs., 37 refs.

Chlorothiazide was employed to treat 480 episodes of cardiac decompensation in 419 patients, aged 5 to 80 years. The precipitating cause of the cardiac failure was rheumatic heart disease in 198, hypertension in 87, coronary sclerosis in 52, and miscellaneous heart disease, including cor pulmonale and congenital abnormalities, in 82. The diuretic was given daily in amounts varying from 0.5 to 4 g. per day, the average dose being 1.5 g. Potassium chloride was also administered in an average daily dose of 1.25 g. although one patient was given as much as 10 g. daily. The course of treatment varied from 1 to 29 days (average 8 days) during which the urinary output ranged from 0.5 to 6 litres per day. Other drugs given were digitalis and prednisone, while on 31 occasions mercurial diuretics were administered intravenously in addition.

The average weight loss was 2.8 kg. The results were considered to be excellent in 61%, mediocre in 32%, while in 7% the patient's condition deteriorated. On the whole there was an improvement in renal excretory capacity in those patients in whom renal function had been impaired and only one patient showed serious hypokalaemia, which was rapidly corrected by a daily dose of 10 g. of potassium chloride. The authors conclude that chlorothiazide is superior to mercurial diuretics in 53% of such cases, equal to them in 22%, and less effective in 25%.

G. S. Crockett

VALVULAR DISEASE

293. Complete Replacement of the Mitral Valve. Successful Clinical Application of a Flexible Polyurethane Prosthesis

N. S. BRAUNWALD, T. COOPER, and A. G. MORROW. *Journal of Thoracic and Cardiovascular Surgery* [J. thorac. cardiovasc. Surg.] 40, 1-11, July, 1960. 13 figs., 6 refs.

Surgical reconstruction of a defective mitral valve is not always practicable if there is loss of substance or rigidity which precludes effective closure. The authors of this paper from the National Heart Institute, Bethesda, Maryland, describe a technique in which damaged valve leaves are excised and replaced by an artificial valve. The prosthesis consisted of a polyurethane compound reinforced with "dacron" and shaped in a mould cast made from a normal necropsy specimen. The artificial leaves had sufficient flexibility to imitate normal valve action, but to prevent them being blown inside out artificial chordae made of "teflon" tape were added and these were passed in the region of the papillary muscles and sutured with the correct degree of tension to the outside of the left ventricle.

The operation for complete valve replacement was carried out on 2 patients with a successful result in one.

Perfusion was required before the left atrium could be opened and the mitral valve exposed. The damaged valve was excised, leaving a small rim, and the artificial chordae were passed through the left ventricular wall and pulled until the "valve" was in place, where it could be sutured to the annulus or cut valve rim. The difficulty of procuring the correct tension of the chordae to allow adequate valve closure was overcome by adjusting the chordae by palpation after the atrium had been partly sutured. A finger was inserted into the atrium and the caval tourniquets relaxed so that the valve function under approximately normal conditions could be assessed.

T. Holmes Sellors

294. Partial Replacement of the Mitral Valve with Synthetic Fabric

H. KING, CHIEN SHENG SU, and J. G. JONTZ. *Journal of Thoracic and Cardiovascular Surgery* [J. thorac. cardiovasc. Surg.] 40, 12-16, July, 1960. 2 figs.

At Indiana University School of Medicine, Indianapolis, experiments were carried out on dogs under cardiopulmonary by-pass to determine whether part or whole of the aortic leaflet of the mitral valve could be replaced by a prosthesis. In some cases a small area of valve was excised and replaced by nylon or "teflon" cloth while in others the chordae were detached and most of the valve excised before replacement. In the first group of small replacements the graft appeared to be satisfactorily incorporated in the valve leaf, but with larger grafts initial success was often succeeded by failure owing to tearing out of the sutures from the chordae after a few days.

This paper illustrates some of the problems of inserting grafts into a continually moving and delicate part of the heart. Suturing was difficult, stitches tended to tear out some days later although the graft did not appear to be under tension at the time of suture, and patches of fabric tended to become more rigid than the valve leaflet.

T. Holmes Sellors

295. The Risks of Deferring Valvotomy in Patients with Moderate Mitral Stenosis

R. G. BANNISTER. *Lancet* [Lancet] 2, 329-333, Aug. 13, 1960. 8 refs.

The author analyses the subsequent history of 105 patients with mitral stenosis, seen at the Brompton Hospital and the National Heart Hospital, London, in whom operation was deferred because symptoms were trivial. All had dominant mitral stenosis, and the mean pulmonary capillary venous pressure was 12 mm. Hg. In 30 patients cardiac catheterization was performed. The average duration of follow-up was 4½ years.

Bacterial endocarditis developed in one patient, systemic emboli in 22, progressive breathlessness in 39, and 43 remained substantially unchanged. Death occurred in 5 of the patients with emboli and 10 of the remainder had residual disability. In the patients with emboli the average age was higher and atrial fibrillation was twice as common as in the remainder of the patients, but emboli also occurred in 5 patients who were in sinus rhythm. Eventually 54 patients underwent valvotomy.

Thus, in this series deferment of operation because of the paucity of symptoms was shown to carry a high risk, since over 20% of patients developed systemic emboli, whether or not they were in sinus rhythm, and 5% died; this is a risk greater than that of the operation itself.

J. R. Belcher

296. Aortic Stenosis

E. W. HANCOCK and P. R. FLEMING. *Quarterly Journal of Medicine [Quart. J. Med.]* 29, 209-234, April [received Aug.], 1960. 18 figs., 19 refs.

At Guy's Hospital, London, percutaneous left ventricular puncture was performed in 70 cases of aortic stenosis to assess the severity of the stenosis and to differentiate valvular and subvalvular lesions. Pure aortic stenosis of moderate or severe degree was present in 41 cases, and from a study of these the authors conclude that probably the most useful measurement in the assessment of each case is the calculated aortic valve area. They found that true inversion of the left precordial leads in the electrocardiogram was nearly always present in these cases. The commonest clinical symptoms were dyspnoea, angina, and effort syncope. Another interesting finding was that the increased cardiac output in cases of early aortic stenosis was probably largely taken up by the need to provide an increased coronary circulation to the hypertrophied left ventricle. An anacrotic notch was present in the majority of cases of severe or moderately severe stenosis and this notch seemed to arise as an effect of the high velocity jet in the root of the aorta just beyond the stenosed valve. Contrary to traditional teaching, the cardiac output was rarely found to be low in the early stages of the disease, even when there was evidence of severe obstruction. In addition, the average resting output of the patients with effort syncope was not significantly lower than that of patients without symptoms.

The authors describe 10 cases of mild aortic stenosis, emphasizing the value of the electrocardiographic findings in selecting patients for operation, 10 cases with accompanying regurgitation, and 9 cases of subvalvular stenosis.

J. B. Wilson

297. Surgical Treatment of Pulmonary Stenosis Using Extracorporeal Circulation

F. GERBODE, J. K. ROSS, G. A. HARKINS, and J. J. OSBORN. *Surgery [Surgery]* 48, 58-64, July, 1960. 2 figs., 7 refs.

The exact extent of the malformations in pulmonary stenosis cannot always be determined before operation but an unhurried exposure under direct vision with cardiopulmonary by-pass allows precise determination. This paper from the Stanford University School of Medicine and the Institute of Medical Sciences, San Francisco, describes the surgical treatment of 55 patients with pulmonary stenosis. In 12 patients there were associated septal defects (atrial in 9 and ventricular in 3). A cardiopulmonary by-pass was employed in 29 cases, in 16 of which there was secondary infundibular stenosis due to muscle hypertrophy. There were 3 deaths and 5 patients required re-operation.

The authors state that an emergency, life-saving valvotomy, which may require further enlargement at a later date, is justified in young children with severe pulmonary stenosis. Secondary infundibular obstruction sometimes regresses after valvular division but it may equally cause death soon after operation. If the valvotomy allows some reflux, this additional blood may add to that trapped in the right ventricle. An approach through a short ventricular incision below the valve permits division of the valve, excision of muscle if required, and inspection of the septum. It is also suited to treatment of isolated infundibular stenosis and is valuable in second operations.

M. Meredith Brown

BLOOD VESSELS

298. The Carotid Sphygmogram in Coarctation of the Aorta. (Le sphygmogramme carotidien dans la sténose isthmique de l'aorte)

P. W. DUCHOSAL and R. FEUARDENT. *Schweizerische medizinische Wochenschrift [Schweiz. med. Wschr.]* 90, 875-880, Aug. 13, 1960. 9 figs., 9 refs.

From a preliminary study of normal carotid sphygmograms, carried out at the Cantonal Hospital, Geneva, the authors describe three principal types of sphygmogram dependent on age. (1) A juvenile type, in which there is a sharp upstroke from the baseline to a peak, followed by a fall to the pre-dicrotic notch; (2) an adolescent type, with a first or early peak followed by a second, late peak, the fall now ending at the dicrotic notch; (3) an adult type, in which a sharp upstroke is interrupted by a less steep rise to a late peak which precedes a fall to the dicrotic notch. In all three types the diastolic fall beyond the dicrotic notch appears as the dicrotic wave in the form of a few rapid vibrations, which are more marked in young than in older patients. The authors interpret the initial upstroke as being due to oscillations in the aorta set up by emptying of the ventricles. Filling of the descending aorta occasions the presence of the late systolic peak. The more rapidly the maximum expansion of the aortic reservoir occurs, the earlier and more pronounced does the increase in pressure become visible as a second excursion of the systolic thrust, and vice versa. Progressive loss of expansion of the reservoir with age explains the emergence of the second peak in adolescence and its predominance in adult life.

The authors then studied the carotid sphygmograms of 24 patients, aged from 3 to 56 years, suffering from coarctation of the aorta. Of these patients 13 underwent surgical repair and postoperative sphygmograms were obtained, 9 of the patients being 15 years or younger and the other 4 aged 18, 19, 27, and 41 years respectively. The preoperative carotid sphygmograms revealed a stereotyped picture, independent of age, which showed the following characteristics. (1) A general rounding of the summit of the systolic curve, with the highest point lying between the positions of the normal early and late peaks. The authors consider that the small volume of aorta proximal to the coarctation explains the particular

rounded outline of the summit, while a high pressure in the aortic reservoir causes the late upthrust to overtake the initial one, so that the first peak is not recorded. (2) Small indentations appearing in the upper half of the upstroke or along its rounded summit are thought to be due to retrograde transmission of turbulences originating at the level of the coarctation. (3) Vibrations in the diastolic wave, these being small in the young and absent in the older patients. The postoperative carotid sphygmograms showed a complete return to normal in 10 of the 13 patients. In 2 others aged 19 and 27 respectively the sphygmogram remained abnormal because of technical difficulties experienced at operation; the remaining patient was aged 41 and because of his age complete restoration was not possible, although the operation was successful.

The authors suggest that it is reasonable to assess the degree of surgical success by comparing pre- and post-operative carotid sphygmograms. Preoperative brachial arteriograms were of two types, showing respectively an exaggeratedly rapid up-thrust, or a slow, "stairway" ascent; in neither type was the picture altered postoperatively. After operation, tibial and other arteriograms of the lower limbs showed the most marked return to normality. The authors stress that the carotid sphygmogram, when used as an accessory diagnostic measure, is specific in the diagnosis of coarctation of the aorta in young children, in whom the classic curve characteristic of this condition is not encountered in any other cardiovascular disease. In patients over 25, however, it is non-specific and only confirmatory, for in older patients this curve may be similar to that obtained in hypertension associated with atherosclerosis.

Finally the authors discuss the findings in cases in which stenosis of the aortic valve is associated with coarctation of the aorta, of which they have encountered only 2 instances.

E. S. Wyder

299. The Fate of the Claudicator

A. SINGER and C. ROB. *British Medical Journal* [Brit. med. J.] 2, 633-636, Aug. 27, 1960. 15 refs.

The results of a follow-up study of 359 patients with atherosclerotic disease (excluding those with thromboangiitis obliterans) are reported from St. Mary's Hospital, London. Of these patients, 250 (222 males and 28 females, mean age 58 years) had signs of femoro-popliteal thrombosis and 109 (94 males and 15 females, mean age 53 years) had signs of aorto-iliac thrombosis. More than half of the total number of patients had hypertension, and 18 had diabetes.

In 52 patients with femoro-popliteal thrombosis direct arterial surgery or lumbar sympathectomy was carried out, with improvement in 33 and no change in 19. Of 114 patients in this group who received vasodilator drugs and/or general advice only, 40 improved, 69 were unchanged, and 5 deteriorated. During the follow-up period of 1 to 5 years 41 patients died, 25 of these from myocardial infarction, 6 from cerebrovascular accidents, and 10 from miscellaneous causes. There were 26 further patients with coronary occlusion and 6 with

cerebral thrombosis who survived. Previous episodes of cardiac ischaemia had been noted in 51 of the patients in this group.

In the aorto-iliac group 41 patients improved following surgery and 8 were unchanged. Of 22 treated conservatively 7 improved, 13 were unchanged, and 2 patients later deteriorated. There were 33 deaths in all in this group during the follow-up period, 14 being due to coronary infarction, 4 to cerebrovascular accidents, and 15 to miscellaneous causes.

A total of 70 patients in the series were given anticoagulants; 69% of these were improved, compared with 51% of a "control" series not so treated. The incidence of thrombosis in the opposite leg was 6% in patients given anticoagulants and 7% in the controls.

H. F. Reichenfeld

300. Raynaud's Disease, Raynaud's Phenomenon, and Serotonin

A. HALPERN, P. H. KUHN, H. E. SHAFTEL, S. S. SAMUELS, N. SHAFTEL, D. SELMAN, and H. G. BIRCH. *Angiology* [Angiology] 11, 151-167, June [received Aug.], 1960. 9 figs., bibliography.

The part played by serotonin (hydroxytryptamine) in Raynaud's phenomenon is discussed in this paper from the Angiology Research Foundation, New York, with reference to the findings in 11 female patients (24 to 38 years old), 5 of whom had primary Raynaud's disease while 6 had Raynaud's phenomenon secondary to other conditions. An infusion of serotonin into the brachial artery of healthy subjects and subjects with Raynaud's phenomenon was followed by vasoconstriction in the hand, with digital cyanosis typical of a Raynaud's attack. When this experiment was repeated after intravenous injection of 1-methyl-D-lysergic acid butanolamide, a serotonin antagonist, it was found that in the healthy subjects there was an immediate lessening of the cyanotic areas with an abrupt rise in digital temperature, whereas the subjects with Raynaud's disease showed only the beginnings of a reversal of temperature which was incomplete after 15 minutes.

The authors conclude that in healthy subjects a serotonin-blocking agent only partly and slowly neutralizes the effects of serotonin on the blood vessels and that the role of serotonin in the pathogenesis and therapy of Raynaud's disease remains a promising subject for further study.

I. McLean Baird

301. Raynaud's Phenomenon Treated with Sympathectomy: a Follow-up Study of 28 Patients

K. V. HALL and L. K. HILLESTAD. *Angiology* [Angiology] 11, 186-189, June [received Aug.], 1960. 3 figs., 9 refs.

Upper-limb sympathectomy for Raynaud's phenomenon was carried out in 28 patients at University Hospital, Oslo. The results after a follow-up period of 6 months to 14 years were classified as excellent (permanent and total relief), fair (reduction in disability or modest improvement), or poor (deterioration). Of 33 upper extremities in 19 patients with primary Raynaud's phenomenon the results were excellent in 61%, fair in 24%,

and poor in 15%. However, of 12 upper extremities in 9 patients with secondary Raynaud's phenomenon excellent results were obtained in only one-third.

The authors conclude that patients with secondary Raynaud's phenomenon show a variable response to sympathectomy and that the best results are obtained in young patients with primary Raynaud's disease.

I. McLean Baird

HYPERTENSION

302. **Spastic and Hypertensive Arteriolitis.** (Спастические и гипертензивные артериолиты)
Z. ŽOUSTEK. *Архив Патологии [Arh. Patol.]* 22, 47-51, No. 5, 1960. 3 figs., 12 refs.

In an attempt to account for the histological changes which occur in malignant hypertension the author puts forward the conception of acute hypertensive arteriolitis, suggesting that the hypothetical sequence of events is as follows. Under the influence of vasospasm and increased blood pressure the arterial walls, especially those of the arterioles, become impregnated with fibrin from the blood. The author states that staining with Mallory's phosphotungstic acid-haematoxylin shows this substance to be true fibrin and not the fibrinoid substance of the so-called fibrinoid degeneration occurring in collagen diseases. This is followed by leucocytic infiltration, while later, necrosis of the vascular wall may occur, but the author stresses the difference of this "ordinary" necrosis from the fibrinoid necrosis of collagen diseases. The changes described were observed in both the systemic and the pulmonary circulation. In a number of non-hypertensive cases fibrinous impregnation of the cerebral arteries was observed, these including cases of eclampsia, status epilepticus, uraemic convulsions, and convulsions of the newborn, even though there was no pre-existing high blood pressure.

A. Swan

303. **Effects of Bretylium Tosylate on Blood-pressure, Cardiac Output, and Renal Function in Hypertension**
A. E. DOYLE, J. R. E. FRASER, and P. KINCAID-SMITH. *British Medical Journal [Brit. med. J.]* 2, 422-425, Aug. 6, 1960. 1 fig., 7 refs.

The results obtained at the Royal Melbourne Hospital with bretylium tosylate in the treatment of 25 patients with hypertension who had had troublesome side-effects with mecamlamine or pempidine are reported. These patients represented about a third of all patients treated with ganglion-blocking drugs; in the remainder mecamlamine or pempidine, usually with reserpine and chlorothiazide, was satisfactory. The initial oral dosage of bretylium tosylate was 200 mg. 3 times daily, this being increased by increments of 100 mg. until the systolic pressure was about 140 mm. Hg in the standing position.

The average dosage required for a satisfactory reduction in the blood pressure was 600 mg. (range 200 to 1,200 mg.) 3 times daily. Tolerance developed in 4 patients after an initial response and the dose had to be doubled or trebled. The blood pressure started to fall

about 2 hours after an oral dose, the maximum fall occurring at 3 to 5 hours; the effect had usually passed in 6 to 8 hours. The blood pressure fall was often seen only in the standing position. The effective intravenous dosage was one-fifth to one-tenth of the oral dosage, indicating poor and variable intestinal absorption. The effect of oral doses was found to be inconsistent, especially if the tablets were taken after meals.

Moderately satisfactory blood pressure reduction was achieved in 19 patients, but control was poor in 6. Horner's syndrome and nasal stuffiness often occurred in the first few days of treatment. Pain in the parotid glands developed in 11 patients, tremor with depression in 2, and 4 complained of headache. The renal plasma flow and glomerular filtration rate fell when the blood pressure began to fall, but returned towards normal while the blood pressure still remained low. Studies of cardiac output indicated that bretylium tosylate lowers the blood pressure by preventing effective postural vasoconstriction, rather than by lowering total peripheral resistance.

The authors consider that blood pressure is better controlled with ganglion-blocking drugs, but that bretylium tosylate, with chlorothiazide and reserpine, may be indicated if severe parasympathetic side-effects develop or it is desired to avoid impotence in young men.

David Phear

304. **Clinical and Pharmacological Studies with Guanethidine in the Treatment of Hypertension**
C. T. DOLLERY, D. EMSLIE-SMITH, and M. D. MILNE. *Lancet [Lancet]* 2, 381-387, Aug. 20, 1960. 7 figs., 9 refs.

At the Postgraduate Medical School of London, 80 severely hypertensive patients were given guanethidine by mouth over a period of 9 months, with a "good" result (standing blood pressure of 160/100 mm. Hg or lower) in 34 and a "fair" result (fall in diastolic blood pressure of 20 mm. Hg or more) in 38; this treatment failed in 8 cases (owing to drug resistance and severity of side-effects). The dosage of the drug was 10 to 750 mg. daily, in most cases being between 30 and 120 mg. daily; the initial dose was usually 30 mg. Morning weakness or syncope was common and tended to be associated with effort hypotension. Other side-effects were diarrhoea, bradycardia, parotid tenderness, nasal obstruction, coarse muscle tremor, unexplained gain in weight with oedema, dyspnoea on exertion, fatigue, depression, and failure of ejaculation. Patients previously treated with ganglion-blocking drugs preferred guanethidine. Drug tolerance as seen in the case of bretylium was not a problem. Intravenous injection of up to 40 mg. was associated with skin warmth, flushing, and a small, immediate rise in blood pressure, followed by a fall, which was maximal in 10 to 20 minutes.

Pharmacological studies were carried out with radioactive guanethidine labelled with ^{14}C in the guanidine carbon. Chemical estimations of guanethidine were made by means of a bromocresol-green dye-conjugation method. In rats, subcutaneously injected, guanethidine was recovered in the urine along with three

metabolites closely allied to the parent substance. Excretion of the drug was not influenced by acid-base imbalance. Rats had poor absorption of guanethidine from the alimentary tract. In tissue distribution studies the highest concentration was found in the kidney. In patients, the mean urinary excretion 24 hours after an intravenous dose was 52% and after an oral dose 24%, appreciable excretion continuing up to 3 days after an oral dose. Absorption from the gut was incomplete. There was no evidence of appreciable biliary excretion of guanethidine in a patient who had a cholecystostomy.

K. G. Lowe

305. Comparison of Bretylium Tosylate with Guanethidine in the Treatment of Severe Hypertension

J. M. EVANSON and H. T. N. SEARS. *Lancet* [*Lancet*] 2, 387-389, Aug. 20, 1960. 7 refs.

At Manchester Royal Infirmary the efficacy of two hypotensive agents was compared in 44 patients, 29 of whom had malignant hypertension and 15 had severe benign hypertension (with diastolic blood pressure in excess of 120 mm. Hg). Bretylium tosylate was given to 27 of the patients in an initial dosage of 200 mg. 3 times daily, with increments of 100 mg. until there was a satisfactory response; guanethidine was given to 17 patients in an initial dosage of 10 or 20 mg. daily with increments of 5 or 10 mg. Assessment of clinical response was based on the fall in blood pressure, improvement in symptoms, regression of retinopathy, and severity of side-effects. When 25 of the patients were treated with bretylium in hospital the results were satisfactory in 22, fair in 2, and poor in one, but when they were treated on an out-patient basis the responses were satisfactory in 5, fair in 4, and poor in 16. With guanethidine the results in hospital were satisfactory in 16 and poor in one; with out-patient treatment the responses were satisfactory in 10, fair in 5, and poor in one. Bretylium was much less satisfactory than guanethidine for long-term control, since tolerance rapidly developed with much consequent inconvenience to the patient from frequent changes of dosage and the addition of other hypotensive agents. The maintenance dosage of guanethidine ranged from 5 to 80 mg. daily, the majority requiring about 40 mg.; very few patients needed additional drugs. Troublesome side-effects with bretylium were nasal stuffiness, exertional dyspnoea, severe pain in the parotid glands, diarrhoea, and muscular weakness; with guanethidine they were diarrhoea, parotid pain, and mild exertional dyspnoea. Mental changes occurred in a few cases with both drugs.

K. G. Lowe

306. The Circulatory Effects of Bretylium Tosylate and Guanethidine

S. H. TAYLOR and K. W. DONALD. *Lancet* [*Lancet*] 2, 389-394, Aug. 20, 1960. 1 fig., 7 refs.

Haemodynamic studies were carried out at the Royal Infirmary, Edinburgh, before and after intravenous administration of bretylium (90 to 600 mg.) in 13 patients with uncomplicated hypertension, 22 patients with rheumatic heart disease, and 6 normal subjects, and of

guanethidine (20 to 40 mg.) in 5 patients with uncomplicated hypertension. With bretylium there was flushing, nausea, and diplopia, and a rapid fall in blood pressure which, in the normal and most of the hypertensive subjects, was followed by a rise above the pre-injection level. In the rheumatic group there was a consistent hypotensive effect with very small doses. The normal and hypertensive subjects showed a rise in resting ventilation and cardiac output without tachycardia. The authors observed a fall in blood pressure during moderate exercise (10 mm. Hg mean fall in normal subjects and 20 mm. Hg mean fall in the hypertensives) and a fall in systemic vascular resistance probably due to loss of effective vasoconstriction in non-exercising muscle, as shown by regional blood flow studies. Bretylium reduced renal blood flow and glomerular filtration rate but had no marked effect on the extraction ratio of para-aminohippurate. In the normal and hypertensive patients and also the rheumatic patients without pulmonary hypertension bretylium raised the pulmonary arterial pressure and vascular resistance.

Guanethidine differed from bretylium in that it did not cause increased cardiac output, a swing from hypotensive to hypertensive effect, or increased pulmonary vascular resistance. Moreover, it did not cause such severe exercise hypotension.

[Those interested will require to study this paper in detail.]

K. G. Lowe

307. The Effects of Prolonged-action Guanethidine on Renal Function in Hypertensive Patients. (Die Wirkung langdauernder Guanethidin-Verabreichung auf die Nierenfunktion von Hochdruckkranken)

C. BARTORELLI, N. GARGANO, D. REGOLI, and A. ZANCHETTI. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] 85, 1271-1275, July 9, 1960. 4 figs., 3 refs.

In the investigation here reported from the University of Siena, which was designed to evaluate the effects of a long-acting preparation of guanethidine ("ismelin") on the renal function of hypertensive patients, the following tests were carried out on 12 patients whose median blood pressure before treatment lay between 130 and 164 mm. Hg: PAH-clearance and inulin-clearance to test the effective renal plasma flow and glomerular filtration rate respectively, the filtration fraction, and the excretion rates of sodium, potassium, and water. These tests were carried out before, and again between 8 and 30 days after, the start of treatment, both with the patient in the supine position and tipped-up to an angle of between 15 and 45 degrees.

The effective renal plasma flow and glomerular filtration rate which were already below normal [as might have been expected in these severely hypertensive patients] were further reduced by ismelin therapy, this reduction being particularly marked in the tipped-up position and associated with the orthostatic hypotensive action of the drug. Marked reductions in sodium and water excretion and, to a lesser extent, potassium excretion, were also noted, but without affecting the serum electrolyte levels.

H. F. Reichenfeld

Clinical Haematology

308. Data on Linkage in Man: Ovalocytosis, Sickling and the Rhesus Blood Group Complex

C. A. CLARKE, W. T. A. DONOHUE, R. FINN, R. B. MCCONNELL, P. M. SHEPPARD, and D. S. M. NICOL. *Annals of Human Genetics* [Ann. hum. Genet.] 24, 283-286, July, 1960. 2 figs., 5 refs.

The authors report, from the University of Liverpool, the pedigrees and details of two families in which the genes controlling ovalocytosis and the Rhesus blood group complex were shown to be linked; the families were discovered by chance during other blood group research. In Family I the ovalocytosis-affected propositus was a West African negro who had married an unaffected Irish woman; they had 3 affected and 5 unaffected children. Inquiries in Sierra Leone (by Nicol) elicited the information that the propositus had an affected sister who also had the sickle-cell trait; she was married to an unaffected man and had 5 children, including non-identical twins. In this sibship one of the twins had ovalocytosis, 3 of the children (including the other twin) had the sickle-cell trait, and one had both the sickle-cell trait and ovalocytosis. A maternal cousin of the propositus also had the sickle-cell trait and the father of the propositus was a probable carrier of the gene controlling ovalocytosis. Linkage between ovalocytosis and the cDe (R_0) genotype combination is clearly shown in the family tree and formal scoring of the pedigree was consistent with total linkage; there were no cross-overs in the 9 persons in whom recombination could have been detected. When the data from this family were combined with those of the 4 other large families reported by Morton (*Amer. J. hum. Genet.*, 1956, 8, 80) the cross-over value for the 5 families was calculated to be $2.90\% \pm 2.02\%$. There is some evidence in the pedigree of linkage between the genes for the sickling-cell trait and blood group P, but as the observation could easily have arisen by chance and as the authors were unable to find any previous linkage studies involving both this blood group and the sickling-cell trait, further studies are clearly indicated.

The members of Family II were less cooperative and less information was obtained. The affected propositus was a woman aged 65 from North Wales who had married an unaffected man and had had 5 children; 4 of these were tested and one was shown to have abnormal erythrocytes. From 2 of the woman's unaffected children there were 7 grandchildren, but only 2 of these could be tested and both were unaffected. The affected daughter of the propositus had one affected and one unaffected child. The pedigree favours linkage between ovalocytosis and the cDe (R_1) combination. There were no cross-overs in the 5 persons in whom they could have been detected. It is noted that none of the persons with ovalocytosis in either family had anaemia, jaundice, or other obvious haematological abnormality, but 2 of the children of the

sister of the propositus of Family I had slight anaemia of unknown origin, one being the twin and the other her sister who had the sickling trait as well as ovalocytosis.

E. A. Cheeseman

309. Clinical and Pathogenetic Aspects of Anaemias following Gastrectomy. (Некоторые результаты изучения клиники и патогенеза агастрических анемий)

A. A. BAGDASAROV, P. M. AL'PERIN, M. JA. ANŠEVIC, and R. I. RODINA. *Терапевтический Архив* [Ter. Arh.] 32, 11-17, July, 1960. 10 refs.

The anaemia which often follows gastrectomy or functional exclusion of the stomach may appear clinically in the form of either iron-deficiency anaemia or vitamin-B₁₂-deficiency anaemia, or it may be of mixed type. The typical picture most often develops after total gastrectomy, but sometimes also after subtotal or even partial gastrectomy. From their investigation of 110 post-gastrectomy patients the authors report as follows. In the early stages the anaemia is hypochromic or normochromic (and may be already macrocytic), while later it becomes hyperchromic macrocytic, not unlike Addisonian pernicious anaemia. Occasionally, in the very late stages, total gastrectomy is followed by the development of megalocytic anaemia identical with the Addisonian type. In a few cases the development of anaemia is preceded by neurological disturbances. In a majority of cases the bone marrow is normo- or megaloblastic, with the erythrocyte series predominating and showing evidence of arrest at the erythroblast stage. In 10 of the authors' cases the bone marrow contained megaloblasts. Agastric anaemia is more common and appears after gastrectomy earlier in cases of carcinoma of the stomach than in cases of peptic ulcer; it also more frequently follows total than subtotal or partial gastrectomy. Hypochromic agastric anaemia is due to lack of iron resulting from the absence of hydrochloric acid. Later on, a progressive deficit of vitamin B₁₂ leads to abnormalities of erythropoiesis and neurological disorders.

Estimation of the serum iron level in 32 patients at various periods after the operation and again after treatment showed that before treatment this level was low in 19 (28 to 56 $\mu\text{g.}$ per 100 ml.), normal in 9 (84 to 112 $\mu\text{g.}$ per 100 ml.), and high in 6 patients, the high values being observed mainly in patients with hyperchromic anaemia. Treatment with iron preparations alone induced a rise in the serum iron level in 10 of these 32 patients. Vitamin B₁₂ metabolism was studied in 62 patients at various periods after gastrectomy and was found to be low (below 0.6 $\mu\text{g.}$ per ml.) in all but 2 patients subjected to total or subtotal gastrectomy and in 28 of 38 patients after partial gastrectomy. Injections of vitamin B₁₂ quickly raised the blood concentration of the vitamin as well as its urinary excretion (to between 110 and 4,264 $\mu\text{g.}$ in 24 hours). Latent agastric anaemia can be demonstrated by estimating the serum

iron and vitamin B₁₂ concentrations in the blood and urine before and after a single large parenteral injection of each substance. Another factor concerned in the development of anaemia may be a disorder of protein metabolism, as indicated by the finding of hypo-albuminaemia and even hypoproteinaemia after gastrectomy. Treatment should therefore include transfusions of whole blood and packed erythrocytes, administration of iron and vitamin B₁₂, while in cases of marked protein deficiency without anaemia transfusions of plasma are indicated. Even in cases of hypochromic post-gastrectomy anaemia the treatment should include vitamin B₁₂ as well as iron and ascorbic acid. The authors suggest that vitamin B₁₂ should be administered in a dosage of 100 to 200 µg. on alternate days to a total dose of 2,000 µg. to all patients with agastric anaemia whatever its clinical form, while its administration to all patients after total, subtotal, or partial gastrectomy would be of great prophylactic value.

S. W. Waydenfeld

parts of unpurified hog pylorus, 21 of them having also been given folic acid. The blood count in all except one of the patients was normal, the one exception showing a mild iron-deficiency anaemia. However, 10 patients had very low serum vitamin B₁₂ levels for which no pathological explanation was available. Of 7 patients in whom the low value was, on their own admission, due to carelessness in maintaining the treatment 2 had serious neurological signs and in one neurological changes initially present had worsened. Of the remaining 3 patients one had taken the treatment so irregularly that its value could not be estimated, but in the other 2 the only likely explanation was that they were unable to absorb vitamin B₁₂, since even greatly increased doses of the test mixture failed to raise the serum level of this vitamin. The authors thus agree with those who maintain that, at present at least, crude preparations are better than purified ones for the oral treatment of pernicious anaemia.

M. C. G. Israëls

310. Oral Treatment of Pernicious Anaemia with Low Doses of H.P.P./1

F. S. MOONEY and J. G. HEATHCOTE. *Lancet* [Lancet] 2, 291-292, Aug. 6, 1960. 2 figs., 5 refs.

Doubt has been expressed whether the vitamin B₁₂ (cyanocobalamin)-peptide complex (H.P.P./1) is any more effective than crystalline vitamin B₁₂ in the oral treatment of pernicious anaemia. The authors describe the treatment of 6 patients with pernicious anaemia, seen at St. Helens Hospital, Lancashire, who responded satisfactorily to small oral doses of H.P.P./1. The daily dose, in terms of vitamin B₁₂ content, ranged from 4.5 to 20 µg. For a preliminary control period 3 patients were given oral crystalline vitamin B₁₂, but without any haematological improvement. Normal haemoglobin and haematocrit levels were maintained in 4 patients with a daily dose of the complex of 5 µg. or less and in the remaining 2 patients with daily doses of 7 and 10 µg., the period of observation ranging from 138 to 528 days. The authors consider that by giving small doses of H.P.P./1 after a control period of treatment with crystalline vitamin B₁₂ orally, they have met criticism of their previous work (*Lancet*, 1958, 1, 982; *Abstr. Wld Med.*, 1958, 24, 276).

J. L. Markson

311. Oral Maintenance Treatment of Pernicious Anaemia with a Crude Preparation of Beef Liver and Total Hog Pylorus (Hepaforte). [In English]

U. EVALDSSON, A. GRÖNBERG, and A. KILLANDER. *Acta medica Scandinavica* [Acta med. scand.] 167, 139-148, 1960. 4 figs., 12 refs.

It is well known that patients with pernicious anaemia who have been treated with oral mixtures of crystalline vitamin B₁₂ (cyanocobalamin) and purified preparations of intrinsic factor made from hog pylorus or duodenum tend to relapse over a period of years and become refractory to treatment. At the Central County Hospital, Vänersborg (University of Uppsala), Sweden, the authors have therefore re-examined a group of 65 patients who had been treated for 3 to 17 years with an oral preparation containing 10 parts of crude bovine liver and 8.5

312. Cortisone and Skin Sensitivity to Tuberculin in Reticuloses

G. H. FAIRLEY and J. Q. MATTHIAS. *British Medical Journal* [Brit. med. J.] 2, 433-436, Aug. 6, 1960. 14 refs.

The object of this study was to determine whether patients with malignant lymphoreticular disease, who are frequently insensitive to tuberculin, would become sensitive when cortisone was injected with tuberculin. Skin sensitivity to 10 and to 100 tuberculin units (t.u.) of purified protein derivative (P.P.D.) was determined in 138 patients with reticuloses, 43 patients with carcinoma, and 116 control subjects at St. Bartholomew's Hospital, London. The injection of tuberculin and cortisone was prepared by mixing equal volumes of the appropriate P.P.D. solution and a suspension containing 1.25 mg. of cortisone acetate.

Previous reports that tuberculin sensitivity is depressed in the reticuloses were confirmed, 45% of such patients being insensitive, compared with 18% of those with carcinoma and 12% of the controls. Cortisone tended to reduce the area of the reactions in patients in all 3 groups who were sensitive to 10 or 100 t.u.

In patients who were insensitive to tuberculin, 8% of those with reticuloses, 7% of the controls and none of those with carcinoma gave a positive reaction with tuberculin with cortisone. This is in contrast to the findings of Citron and Scadding (*Quart. J. Med.*, 1957, 26, 277; *Abstr. Wld Med.*, 1958, 23, 88), that in sarcoidosis and tuberculosis 50% of patients who are insensitive to 100 t.u. become sensitive when cortisone is injected with the tuberculin.

These results support the view that the mechanism of suppression of tuberculin sensitivity in sarcoidosis is different from that in the reticuloses. Probably both steroid therapy and increasing severity of the disease contribute to the marked suppression of tuberculin sensitivity in these patients. In a patient who is insensitive to tuberculin the development of sensitivity when cortisone is added suggests, but is not diagnostic of, sarcoidosis rather than one of the reticuloses.

A. W. H. Foxell

Respiratory System

313. **Old Age and Hypoxia.** (Старость и гипоксия) N. N. SIROTININ. *Клиническая Медицина [Klin. Med. (Mosk.)]* 38, 72-74, Aug., 1960.

Temporary partial hypoxia occurs in various circumstances throughout life from birth to death, but the elderly are particularly subject to hypoxia as a result of the various ailments common to old age. There is a correlation between the changes in the higher nervous activity in old age and the concomitant hypoxia. Thus, it has been shown that conditioned reflexes in older dogs are less stable than in younger animals. Also in non-acclimatized subjects high altitudes, because of the reduced atmospheric oxygen content, deeply affect the higher nervous activity and memory.

These experimental findings have been confirmed by the favourable results obtained with oxygen therapy in elderly people. However, acclimatization to high altitudes, once achieved, favours longevity. The well-known longevity of Bulgarian shepherds is due, not to the daily consumption of yoghurt as was erroneously assumed by Metchnikov, but to the high altitude of the pasture lands where a large part of their lives is spent.

A. Orley

314. **Respiratory Failure: the Relation between Oxygen Concentrations of Inspired Air and Arterial Blood**

E. J. M. CAMPBELL. *Lancet [Lancet]* 2, 10-11, July 2, 1960. 1 fig., 9 refs.

At the Middlesex Hospital, London, the author has studied in 4 patients with respiratory failure the relation between the oxygen concentration in the inspired air and that in the arterial blood. It was shown that in patients with severe respiratory failure small degrees of O₂ enrichment of the inspired air gave well marked rises in O₂ tension in the blood. In patients with respiratory failure who were in danger of carbon dioxide narcosis the author suggests that O₂ should be given continuously and that the O₂ concentration should be sufficiently controlled to prevent severe respiratory depression and a recurrence of the anoxic state. For such control the inspired oxygen concentration should be given with an accuracy of $\pm 1\%$ in the range of 24 to 35%. It is also recommended that rebreathing of expired air should be avoided if possible.

G. M. Little

315. **A Method of Controlled Oxygen Administration Which Reduces the Risk of Carbon-dioxide Retention**

E. J. M. CAMPBELL. *Lancet [Lancet]* 2, 12-14, July 2, 1960. 4 figs., 2 refs.

In this further paper [see Abstract 314] the author outlines the improved procedure which he has used for administering O₂ to anoxic patients at the Middlesex Hospital, London. Initially, he demonstrated that conventional methods of O₂ administration did not give sufficiently accurate control of the amount of O₂ inspired by patients with respiratory failure, but that the ad-

ministration of air at a high flow-rate, with added O₂, produced the necessary accuracy. He then describes an apparatus employing the Venturi principle in which a jet of oxygen delivers 1.5 to 2 litres of O₂ per minute and entrains some 50 litres of air per minute, thus giving an O₂ concentration of about 24%. If a higher concentration is desired a second tube is used to deliver a further supply of O₂.

G. M. Little

316. **Effects of Cold Air on Respiratory Airflow Resistance in Patients with Respiratory-tract Disease**

R. W. WELLS JR., J. E. C. WALKER, and R. B. HICKLER. *New England Journal of Medicine [New Engl. J. Med.]* 263, 268-273, Aug. 11, 1960. 2 figs., 10 refs.

The authors of this paper from the Peter Bent Brigham Hospital and Harvard University Medical School, Boston, studied the effect of cold air on respiratory airflow resistance in 5 healthy subjects and 20 patients with asthma, bronchitis, or emphysema or a combination of these. The patients were observed before, during, and after inhalation of air at about -30° C. The air was cooled in a heat exchanger and its temperature measured by a thermocouple in the mouthpiece of the inhalation apparatus. Pulmonary airflow resistance was determined by an intra-oesophageal balloon connected to a differential pressure transducer. The resistance was measured as the ratio of pressure change to flow change.

Most of the patients had previously noted respiratory embarrassment in cold environments. The majority of these showed a marked rise in pulmonary airflow resistance when they breathed cold air. The healthy subjects and 5 patients whose breathing was unaffected by cold showed little change in resistance. Inhalation of nebulized isoproterenol prevented the rise in resistance in most of the affected patients. When the cold air was directed across the face or body of the patient and not inhaled, there was no change in lung resistance.

D. Goldman

317. **Mucoviscidosis as a Factor in Chronic Lung Disease in Adults**

A. J. KARLISH and A. L. TÁRNOKY. *Lancet [Lancet]* 2, 514-515, Sept. 3, 1960. 1 fig., 18 refs.

The sweat electrolyte levels have been estimated in 18 healthy individuals and in 48 patients with chronic non-tuberculous lung disease attending the Reading Chest Clinic. Abnormally high sweat values for chloride of 66 to 99 mEq. per litre and for sodium of 83 to 134 mEq. per litre were observed in 11 adults and one child. In 10 of these 12 patients the bronchograms were abnormal. Relatives of 3 patients also had high sweat chloride values. The authors suggest that the condition in these cases may be an incomplete form of mucoviscidosis and that a genetically determined factor may be present in a significant proportion of adults with chronic non-tuberculous lung disease.

I. Ansell

Otorhinolaryngology

318. Tissue Reaction following Reconstruction of the Oval Window in Experimental Animals

R. J. BELLUCCI and D. WOLFF. *Annals of Otology, Rhinology and Laryngology* [Ann. Otol. (St Louis)] 69, 517-539, June [received Aug.], 1960. 15 figs., 3 refs.

The tissue reaction which occurs in the cat's ear after a graft or a foreign substance has been inserted so as to cover up the oval window is reported in this study from Manhattan Eye, Ear and Throat Hospital, New York. In the first series of 9 cats the oval window was covered with a vein graft after the footplate of stapes had been removed. Considerable fibrous reaction around the vein graft was noted. In a further 8 cats "gelfoam" was used instead of a vein graft, and in 3 of these the fibrosis was similar to that occurring after the use of a vein graft. In 2 specimens the basilar membrane could not be identified, and the damage was thought to be due to chemical change. The authors do not consider that the internal ear damage was due to infection, and while they suggest that their results may have a bearing on the latest stapes-footplate operations for otosclerosis, they admit that the reaction may not be the same in man as it is in an experimental animal. *William McKenzie*

319. Indolent, or So-called Serous Otitis Media. Including Combined Allergy and Virus Studies

L. Z. FISHMAN, E. H. LENNETTE, and T. B. DANNENBERG. *Archives of Otolaryngology* [Arch. Otolaryng.] 72, 25-30, July, 1960. 3 refs.

It is suggested that the term "serous otitis media" might be replaced more appropriately by "indolent otitis media". Cases of serous otitis media are characterized by chronic, low-grade, subjective as well as objective ear symptoms without much systemic reaction, although, usually, there is impairment of hearing with inconstant otoscopic signs. Fluid levels or bubbles deep to the drum are pathognomonic of the condition but are present in only about 10% of cases. The authors state that patients have been seen in whom the condition has been overlooked for 6 months; in one case the presence of fluid was demonstrated by diagnostic myringotomy after a delay of 3 years. Myringotomy should be performed in all cases of hearing loss, particularly in children [? in cases of unexplained hearing loss in which aspiration and inflation via the Eustachian tube may be needed to expel the fluid from the middle ear through the incision.] It is held that the effusion is caused by blockage of the Eustachian tube leading to a vacuum in the middle ear, which is corrected by the release of fluid from the surrounding epithelium and capillaries.

The increased incidence of the condition, especially during the last 3 years, has led to the suggestion that this is "a new etiologic entity" resulting from ill-advised antibiotic therapy. However, in many cases

there is no history of any such treatment. Allergy may be responsible in a small percentage of cases. In the majority the fluid is sterile on culture. The authors state that although a viral aetiology could not be demonstrated in 10 cases seen at Kaiser Foundation Hospital, Walnut Creek, California, it is not impossible that a viral infection may be involved in the recent marked increase in incidence of the disease.

F. W. Watkyn-Thomas

320. Sudden Deafness: Five Cases Treated with Anticoagulants

A. V. B. BOLOGNESI. *Archives of Otolaryngology* [Arch. Otolaryng.] 72, 31-40, July, 1960. 5 figs., 21 refs.

The treatment of 5 cases of sudden unilateral deafness is described in this paper from the Department of Otolaryngology, State University of New York. In all the cases it was possible to exclude injury, infection, intracranial lesion, and Ménière's disease; only in one was there any vestibular disturbance. Anticoagulant therapy with heparin and warfarin was given with complete recovery of function in 3 patients, and partial, temporary improvement in one; there was no improvement in hearing in the involved ear in the remaining case. It is suggested that the most probable cause of the sudden deafness was spasm or thrombosis of the vessels supplying the organ of Corti.

F. W. Watkyn-Thomas

321. Serial Studies of the Onset and Progression of Drug-induced Cochlear Damage in Cats: a New Electrophysiologic Method

F. B. SIMMONS, R. GALAMBOS, and J. P. ALBRITTE. *Archives of Otolaryngology* [Arch. Otolaryng.] 72, 233-239, Aug., 1960. 3 figs., 12 refs.

This paper from the Walter Reed Army Institute of Research, Washington, D.C., describes a new electrophysiological method for continuous evaluation of progressive cochlear damage due to substances toxic to the ear. In the experiments reported electrodes were permanently implanted on the round window in cats, which then received various dosages of streptomycin, dihydrostreptomycin, and neomycin for periods up to 2 months. The cochlear microphonics were measured at regular intervals; it is acknowledged that although this measurement of electric potentials is not a measurement of hearing, nevertheless the two measurements can be "suggestively correlated". In the cats given streptomycin and dihydrostreptomycin signs of vestibular damage regularly preceded signs of cochlear damage. This finding is at variance with the generally held view, based on clinical evidence, that in man dihydrostreptomycin primarily damages the cochlea. Neomycin, which was found to be the most damaging to the cochlea and the most generally toxic, had the least effect on the vestibule.

F. W. Watkyn-Thomas

Endocrinology

THYROID GLAND

322. Evidence for Genetic Predisposition to Formation of Thyroid Autoantibodies (Preliminary Communication)

R. HALL, S. G. OWEN, and G. A. SMART. *Lancet* [Lancet] 2, 187-188, July 23, 1960. 15 refs.

In this preliminary communication the authors report from the Royal Victoria Infirmary, Newcastle upon Tyne, the incidence of auto-antibodies in the relatives of 11 patients with autoimmune thyroid disease. Examination of 39 out of the 44 known siblings of these patients showed that 22 (56%) had auto-antibodies, in 9 cases against thyroglobulin, in one against thyroid microsomes, and in 12 against both; of these 22 siblings 11 had no clinical evidence of thyroid disease, but of the others 7 had an enlarged thyroid gland, 2 were myxoedematous, and 2 had undergone thyroidectomy for thyrotoxicosis. Further, 5 out of 10 children and 2 parents of the propositi also had auto-antibody.

These observations suggest that auto-antibodies are inherited as a Mendelian dominant. The higher incidence of such antibodies in the sisters of the propositi, although not statistically significant, raises the possibility of partial sex limitation. The authors note that these findings are in keeping with the occasional familial incidence of myxoedema and Hashimoto's thyroiditis. They speculate whether the basic genetic abnormality involved the thyroid gland and allowed access of intracellular and intrafollicular material to the antibody-producing system, or whether it was related to increased secretion of pituitary thyrotrophic hormone.

G. L. Asherson

323. Autoimmunity in Human Thyroid Disease

I. R. MACKAY and B. T. PERRY. *Australasian Annals of Medicine* [Aust. Ann. Med.] 9, 84-92, May [received July], 1960. 2 figs., 35 refs.

A precipitin, which is detected most sensitively by a haemagglutination technique, and a complement-fixing antibody have been identified in the serum of patients suffering from thyroid disease. Evidence obtained during a study at the Walter and Eliza Hall Institute of Medical Research, Melbourne, of serological reactions in some 170 patients with thyroid disease and a similar number of control subjects suggested that the antigen responsible for the haemagglutinating antibody was thyroglobulin. Identical titres of the antibody were found in each serum, whether thyroglobulin or the more usual crude thyroid extract were used as the test antigen.

Titres of over 1:100 were found in 4% of control subjects, 14% of patients with simple goitre, 47% of those with thyrotoxicosis, and 72% of patients with Hashimoto's disease. Analysis of the thyrotoxic cases failed to show an obvious correlation between any one

of the clinical features and the occurrence of a high antibody titre. Patients treated with radioactive iodine, however, showed a reduced incidence of agglutinating antibody compared with those treated by surgery.

Significant titres of the complement-fixing antibody, the corresponding antigen to which is found in the thyroid glands of certain thyrotoxic patients, were found less frequently in all groups. However, the distribution among the various clinical groups of the frequency of raised titres was similar to that of the agglutinating antibody.

Sera from a group of patients with various diseases not involving the thyroid gland were also examined. Raised titres of the haemagglutinating antibody were noted in 16% of patients with active chronic hepatitis and in 15% of those with systemic lupus erythematosus. The authors also briefly report 11 cases in which hepatitis or one of the forms of systemic connective tissue disorder was complicated by coincident thyroid disease.

In the discussion it is suggested that in chronic thyroiditis these features of autoimmunization are the result rather than the cause of the thyroid disorder. The authors consider that cell-borne antibody, of the type seen in delayed hypersensitivity states such as the tuberculin reaction and the rejection of homografts, may be more particularly implicated in the aetiology of thyroiditis.

H.-J. B. Galbraith

324. Complement Fixation with Extract of Normal Thyroid Gland: Its Occurrence in Sera from Patients with Thyroid Disease and in Other Conditions

E. HACKETT, M. BEECH, and I. J. FORBES. *Australasian Annals of Medicine* [Aust. Ann. Med.] 9, 93-98, May [received July], 1960. 13 refs.

In addition to the complement-fixing antibody which reacts specifically with an antigen obtained from the thyroid glands of certain thyrotoxic subjects, a complement-fixing antibody has also been described which reacts with extracts of many tissues, including tissue from normal thyroid gland. The latter, normal thyroid (N.T.) antibody, has been found in patients both with and without obvious thyroid disorder. The authors of this paper from the University and the Institute of Medical and Veterinary Science, Adelaide, have studied the incidence of the complement-fixing N.T. antibody in the sera of over 1,000 patients and of 164 healthy subjects. Complement was fixed by sera from 24% of patients with thyroid diseases and from 2% of the controls. The incidence of the complement-fixing N.T. antibody was also increased in systemic lupus erythematosus, liver-cell disease, syphilis, and virus infections. Quite high titres were recorded both in the non-thyroid as well as in the thyroid disorders. With the exception of 2 cases of thyroid disease, every serum which fixed complement with extracts of normal thyroid also reacted with extracts

of at least one other visceral tissue (liver, kidney, adrenal glands, or lung).

All sera from patients with thyroid disease which fixed complement with N.T. extract also fixed complement with thyrotoxic (T.T.) antigen. On the other hand, 50% of patients with T.T. antibodies failed to react with N.T. There was no correlation between the occurrences of N.T. antibody and of the thyroglobulin haemagglutinating antibody. To ensure that the fixing of complement by a serum with extracts of thyrotoxic gland is due to the specific T.T. and not to the non-specific N.T. factor, the authors suggest that similar tests should be carried out on the serum with each of the other 4 tissue extracts. Only if these last tests give negative results can the presence of T.T. antibodies be assumed with confidence.

H.-J. B. Galbraith

325. Precipitin Tests for Auto-immunizing Thyroiditis

D. WATSON. *Australasian Annals of Medicine* [Aust. Ann. Med.] 9, 99-102, May [received July], 1960. 1 fig., 18 refs.

In this paper from the Royal Women's Hospital, Melbourne, the author describes in detail two techniques for the examination of serum for the presence of the precipitin found in thyroid disease. The first is a modification of the standard agar diffusion tube method, while the second is an electrophoretic method. For the latter, a solution of antigen (a dilute thyroid extract and a 1% solution of thyroglobulin gave identical results) is placed on the strip 4 to 5 cm. behind the serum. A positive result is indicated by a deeply-staining band within or adjacent to the region of the γ -globulin fraction.

All except one of 25 patients with Hashimoto's disease gave a positive precipitin reaction, although in a few instances this was not found until after treatment had started. These figures are an improvement on those in all previous reports of the results of precipitin testing in thyroiditis. The electroprecipitin method appeared to be slightly the more sensitive. Positive results were obtained in only 2 of 11 myxoedematous subjects and in 1 of 3 patients with thyroid cancer. No positive results were obtained in the remaining 37 cases of thyroid disease or with the 46 control sera. The precipitin tests provided a more satisfactory diagnostic indicator than did study of the serum protein level; only 11 of 20 patients with Hashimoto's disease showed abnormalities in the electrophoretic strip or in the common empiric flocculation tests. Furthermore, in 8 of 23 patients with other thyroid disorders there was some disturbance of the serum protein pattern.

H.-J. B. Galbraith

326. The Treatment of Toxic Nodular Goiter with Radioactive Iodine: 10 Years' Experience with 436 Cases

M. ELLER, S. SILVER, S. B. YOHANEM, and R. L. SEGAL. *Annals of Internal Medicine* [Ann. intern. Med.] 52, 976-1013, May, 1960. Bibliography.

In the 10-year period 1945-54 about 2,000 patients with hyperthyroidism were treated with radioactive iodine (^{131}I) at the Thyroid Clinic, Mount Sinai Hospital, New York, and in the present paper 1,603 cases for which adequate data were available are analysed and the

relevant literature is reviewed. Nodular goitre was present in 436 cases, a single nodule being palpated in 127. Treatment was with a single dose of ^{131}I , based on a tracer dose, calculated to deliver about 8,000 rads. Further doses were given if the patients were still hyperthyroid after 2 to 3 months. The authors state that 35 to 45% of all their patients—that is, both those with nodular goitre and those with diffuse goitre—were treated within a year of toxic symptoms being noted, and that in both groups 92% were permanently cured and 8% rendered myxoedematous. Patients with nodular goitre tended to require longer treatment and a slightly higher total dosage of ^{131}I .

The authors conclude that the ability of the toxic nodular goitre to take up ^{131}I is only slightly less than that of toxic diffuse goitre and that solitary nodules respond well; substernal goitres may be successfully treated with ^{131}I . It was noted that eye signs were more common in cases of diffuse enlargement; after treatment with ^{131}I there was improvement, although the eye signs did not disappear. Atrial fibrillation and heart failure were more frequent in patients with nodular goitre than in those with diffuse, but in both groups there was a satisfactory response to treatment. In all the patients in this series the hyperthyroidism was satisfactorily controlled with ^{131}I alone.

B. M. Ansell

327. Radioactive Iodine (^{131}I) in the Postoperative Treatment of Thyroid Cancer

W. H. BLAHD, R. A. NORDYKE, and F. K. BAUER. *Cancer* [Cancer (Philad.)] 13, 745-756, July-Aug., 1960. 3 figs., 49 refs.

The authors report their experience since 1949 of the postoperative treatment with radioactive iodine (^{131}I) of cancer of the thyroid. Between 1949 and the early part of 1959, 63 patients with histologically proved carcinoma of the thyroid were referred to the Radioisotope Service, Veterans Administration Center, Los Angeles, and of these 31 received therapeutic doses of ^{131}I , 26 being followed up for more than one year.

The method of treatment was as follows. Administration of thyroid extract was discontinued for 3 weeks, the patients being then given 10 U.S.P. units of thyrotrophic hormone daily for 7 days before a test or treatment with ^{131}I was carried out. A routine treatment dose of 100 mc. of ^{131}I was given if any abnormal uptake was detected by scanning or by estimation of urinary excretion of a tracer dose. Treatment with ^{131}I in doses of 100 mc. was given regularly every 3 to 4 months until no abnormal uptake was detected, even after injection of thyrotrophic hormone. The hormone was administered (more recently as triiodothyronine) in maximum tolerated amounts continuously except for the 72-hours before a ^{131}I test and before subsequent treatment.

Details are given of all the cases and scintigrams showing the effect of thyrotrophic hormone administration are reproduced. It is suggested that thyroidectomy should be first performed, even when the tumour is known to be inoperable, that thyrotrophic hormone is useful in enhancing uptake, that 100 mc. is a safe optimal treatment dose, and that thyroid hormone should be given in addition to other treatment.

K. E. Halnan

328. Survival of Patients with Cancer of the Thyroid Gland

P. MUSTACCHI and S. J. CUTLER. *Journal of the American Medical Association [J. Amer. med. Ass.]* 173, 1795-1798, Aug. 20, 1960. 8 figs., 5 refs.

Almost all new cases of cancer diagnosed in the State of Connecticut are registered centrally, and in the present paper 283 cases of thyroid cancer which were registered in the 16 years up to 1951 are reviewed. The diagnosis was confirmed histologically in 251 (89%) of the cases, the non-papillary form of the disease being twice as common as the papillary. The survival rate in these patients, regardless of the treatment received or the causes of death, are analysed and compared with the expected survival periods, calculated for each patient from the national statistics. The duration of follow-up varied from *nil* to 19 years. In patients in whom the diagnosis was not confirmed histologically mortality was higher during the first year, but thereafter the pattern was similar to that in patients with histologically confirmed disease. The remaining analyses are concerned with the histologically confirmed cases only.

The age distribution and the relative frequency of the histological types were similar in the 62 male and 189 female patients. The mortality, however, was much higher among the men, only 50% of these surviving over 18 months, whereas 50% of the women survived for more than 6 years. One possible implication of these findings is that the factors maintaining activity of thyroid cancer differ from those initiating the tumour. Women with papillary lesions had a very much better outlook than those with non-papillary cancer. There was less disparity between the survival rates in men with the 2 histological types. As might be expected, in cases of cancer which had apparently not spread outside the thyroid gland the prognosis was better than in cases with metastasized lesions. In practically every comparison, the greatest disparity in mortality occurred during the first year; thereafter, the different influences mentioned had little effect upon the survival rates.

H.-J. B. Galbraith

ADRENAL GLANDS

329. The Effect of Testosterone on Corticosteroids in Surgical Trauma: Studies in Man

L. L. SMITH, R. W. STEENBURG, U. F. GRUBER, A. J. KAALSTAD, and F. D. MOORE. *Journal of Clinical Endocrinology and Metabolism [J. clin. Endocr.]* 20, 919-928, July, 1960. 2 figs., 21 refs.

The effect of pretreatment with testosterone on the adrenocortical response to surgery was studied in 5 patients undergoing subtotal gastrectomy. Testosterone propionate was administered intramuscularly or intravenously in doses of 40 to 200 mg. per 24 hours for 1 to 5 days prior to surgery. Plasma free and conjugated corticosteroid concentrations were measured before, during and following operation. The 24-hour urinary excretion of corticosteroid and ketosteroid was also measured. Five other patients who were undergoing gastrectomy but who were not pretreated with testosterone served as controls. Pretreatment with testosterone did not cause a demonstrable alteration in the concentrations of plasma free or conjugated corticosteroid nor in the urinary excretion of corticosteroid or ketosteroid, during and following operation. Pretreatment of normal male volunteers with testosterone failed to alter the ACTH-induced rise in plasma free and conjugated corticosteroid concentrations. Urinary excretion of corticosteroid during and following the administration of ACTH was the same in untreated volunteers as in the same subjects following pretreatment with testosterone propionate.—[Editorial summary.]

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330. Water Diuresis in Adrenal Cortical Insufficiency

A. E. THOMSON, E. G. BROWNELL, and G. R. CUMMING. *Annals of Internal Medicine [Ann. intern. Med.]* 52, 949-959, May, 1960. 3 figs., 20 refs.

In this paper from the University of Manitoba, Winnipeg, the authors report a study of the value of the water-loading test of Oleesky (*Lancet*, 1953, 1, 769; *Abstr. Wld Med.*, 1953, 14, 497) in the assessment of adrenal cortical insufficiency. Up to one litre of water is ingested by the patient over a 20-minute period, samples of urine being collected every 20 minutes for 2½ hours. The rate of excretion is calculated for each time period, and if the maximum urine flow obtained during this period is less than 4 ml. a minute the procedure is repeated the following day when the patient is given 100 ml. of cortisone before ingesting the water.

Over a 5-year period this test was carried out in 238 patients suffering from a variety of disorders. Of 20 patients in whom Addison's disease was suspected on clinical grounds and 8 with hypopituitarism, 25 showed impaired water diuresis if cortisone was not administered; in the remaining 3 a normal response to water loading was observed only after salt repletion. False positive results were obtained in 2 patients with congestive cardiac failure and in one who had undergone right nephrectomy for hydronephrosis. The authors suggest that this procedure is relatively safe and that with adequate precautions to ensure bladder emptying and correction of salt depletion it is a useful clinical index of adrenal cortical insufficiency in patients without cardiac or renal failure.

B. M. Ansell

331. Addison's Disease without Pigmentation. (Об аддисоновой болезни без пигментации)

G. S. ZEFIROVA. *Проблемы Эндокринологии и Гормонотерапии [Probl. Endokr. Gormonoter.]* 6, 37-41, July-Aug., 1960. 46 refs.

Although Addison's disease without pigmentation is rare it does occur, and 2 cases are here described in detail, with a brief review of other reported cases. In all such cases the diagnosis must rest on the clinical symptoms, hypopiesia, the results of the Robinson-Power-Kepler water test and Thorn's eosinophil test, the ascorbic acid balance, the urinary 17-ketosteroid excretion, and the characteristic blood glucose curve.

The pathogenesis of the condition is obscure. Waring and Shizume suggested that a special medulla-stimulating hormone (intermedin) is formed in the pars intermedia

of the hypophysis and that this has an indirect influence on the melanocytes, while adrenaline and noradrenaline suppress them. Lerner regarded this hormone as identical with ACTH. It has been shown that the use of ACTH in the treatment of pan-hypopituitarism may lead to the development of pigmentation of the Addisonian type. Lerner considered that the pigmentation in Addison's disease is due to hypersecretion of ACTH as a result of the adrenal hypofunction. Durlach stated that thyrotrophic hormone contains the melanophore-stimulating factor; but patients with thyrotoxicosis and those with malignant exophthalmos after subtotal thyroidectomy do not as a rule show pigmentation, in spite of the increased secretion of thyrotrophic hormone which occurs. Another factor in the pathogenesis may be ascorbic acid, which in large doses suppresses the pigmentation of Addison's disease, probably by impeding the oxidation of adrenaline. Sayers and fellow-workers demonstrated a diminution in the content of ascorbic acid and cholesterol in the adrenal cortex after administration of ACTH, and suggested that ascorbic acid takes part in the synthesis of the corticosteroids. Further research is called for on the mechanism and pathogenesis of pigment formation in Addison's disease. Both the author's cases responded to treatment with cortisone and deoxycortone acetate.

L. Firman-Edwards

DIABETES MELLITUS

332. Hepatitis Caused by Glipasol (R.P. 2259)—an Antidiabetic Sulphonamide Drug

T. W. DAVIS, R. B. KERR, and A. BOGOCH. *Canadian Medical Association Journal* [Canad. med. Ass. J.] 83, 102-112, July 16, 1960. 5 figs., 19 refs.

The hepatotoxic effects of "glipasol", an oral antidiabetic sulphonamide, which differs from carbutamide and tolbutamide in possessing a thiodiazol rather than a urea nucleus, were studied in 31 diabetic patients at Shaughnessy Hospital, Vancouver. The drug was given in a dosage of 1 to 4 g. daily. A number of liver function tests were carried out before and at intervals during administration of the drug, and needle biopsy of the liver was performed in 5 of the patients.

In 17 patients there was evidence of hepatotoxic effects, which consisted in abnormalities in bromsulphalein excretion, the serum alkaline phosphatase levels, and the urinary excretion of urobilinogen. In addition, 6 of the patients had hyperbilirubinaemia and hepatomegaly, which were associated with splenomegaly in 4. In 5 of these 6 patients liver biopsy showed a combination of parenchymatous damage, focal necrosis, and perivascular and periportal cellular infiltration; in 3 of them examination of the blood revealed eosinophilia.

The incidence of hepatotoxic effects was unrelated to age, duration of diabetes, previous insulin therapy, degree of diabetic control, daily or total dose of glipasol, or duration of administration.

The possible cause of the hepatic derangement is discussed. A direct hepatotoxic effect was unlikely since hepatic function improved in several patients with hepatic

dysfunction when the drug was continued. A hypersensitivity reaction was supported by eosinophilia in 3 patients with a raised serum bilirubin level. Viral hepatitis was considered but discarded in view of the careful syringe sterilization techniques employed.

It is concluded that the incidence of hepatotoxic effects precludes the general clinical use of glipasol.

Gerald Sandler

333. I^{131} Triolein Tolerance Curves in Patients with Diabetes Mellitus: Their Similarity to Those Observed in Myocardial Infarction

H. SANDBERG, B. S. MIN, L. FEINBERG, and S. BELLET. *A.M.A. Archives of Internal Medicine* [A.M.A. Arch. intern. Med.] 105, 866-872, June, 1960. 4 figs., 33 refs.

The radioactive iodine (I^{131})-triolein tolerance curve in diabetes mellitus was studied in 27 diabetics (aged 19 to 86 years) seen at the Philadelphia General Hospital. After an overnight fast the patients received a test meal containing 100 μ c. of I^{131} -triolein and the radioactivity of whole blood and of the fraction precipitated with trichloroacetic acid was measured after 2, 4, 6, 8, and 24 hours. The peak absorption and 24-hour values were within normal limits in 8 patients over 60 years of age who had atherosclerotic cardiovascular complications. These values were slightly, but probably not significantly, raised in 11 patients under 60 years who had no peripheral vascular or cardiac complications. However, peak and 24-hour values were greatly increased in 8 patients under 60 years with peripheral vascular or cardiac lesions, these values being close to those reported previously in patients with myocardial infarction.

M. Lubran

334. Gout and the Serum Uric Acid in Diabetes Mellitus

A. G. BECKETT and J. G. LEWIS. *Quarterly Journal of Medicine* [Quart. J. Med.] 29, 443-458, July [received Sept.], 1960. 2 figs., bibliography.

The serum uric-acid levels in a group of 800 patients with diabetes were lower than the reported figures for non-diabetic subjects. The levels in men were higher than in women. The levels in women increased significantly with age, whereas those for men did not. The lowest values in both sexes were seen in the severe and ketosis-prone types of diabetes, and the highest in patients who were overweight and treated by diet alone. Patients with a family history of gout did not have the higher values normally found in non-diabetic relatives of gouty patients.

A gouty arthritis occurred in 8 patients, but was not associated with the high levels of serum uric acid normally seen in gout. In these patients the gout was mild, as was their diabetes, although they did not escape the vascular complications of diabetes.

It is concluded that diabetes increases the excretion of uric acid by a mechanism as yet unknown. Uric acid is considered to have a mild diabetogenic action. A family history of gout is present more frequently in patients with diabetes than in normal subjects. It is possible that a gene linkage exists between the two diseases.—[Authors' summary.]

The Rheumatic Diseases

335. Streptococcal Infections in Adolescents and Adults after Prolonged Freedom from Rheumatic Fever. I. Results of the First Three Years of the Study

E. E. JOHNSON, G. H. STOLLERMAN, B. J. GROSSMAN, and H. MCCULLOCH. *New England Journal of Medicine* [New Engl. J. Med.] 263, 105-111, July 21, 1960. 2 figs., 18 refs.

The incidence and complications of streptococcal infections were studied in 298 adolescents and adults at the La Rabida Jackson Park Sanitarium or the Northwestern University Medical Clinics, Chicago, who had had rheumatic fever and who, as the result of continuous penicillin prophylaxis, had been free from recurrence for at least 5 years. Prophylaxis was stopped and the patients were examined at least every 2 months, when throat swabs were taken for culture and specimens of serum obtained for determination of the antistreptolysin-O titre. All patients were examined promptly when an illness was reported. Symptomatic streptococcal infections were treated with a single injection of 1,200,000 units of benzathine penicillin intramuscularly. The patients were divided into two groups: 204 adolescents aged 11 to 22 years and 94 adults aged 23 to 70 years.

A total of 115 streptococcal infections occurred over a follow-up period of 572 patient-years, these being symptomatic infections in 22 cases (19% of the total). There was one relapse of rheumatic fever in this group, the patient being inadequately treated by the family doctor. Subclinical asymptomatic infections characterized by a rise in streptococcal antibody titre occurred in 74 patients, these representing 64% of all infections. In 58 patients in this group cultures of throat swabs were positive. There were 6 recurrences of rheumatic fever. Of the streptococcal infections 19 (16% of all infections) were questionable because they were asymptomatic and not associated with a rise in antibody titre, but characterized only by positive throat culture. There were no rheumatic relapses in this group. A significantly higher incidence of infection was observed in the adolescent group (23.2 per 100 patient-years) than in the adults (12.8 per 100 patient-years). This was accounted for by a higher incidence of subclinical infection in the adolescents. However, respiratory infections were reported more frequently in the adults. All 7 rheumatic recurrences were seen in the adolescents, 6 after subclinical infections. There was thus a rheumatic recurrence rate of 1.8% per patient-year in adolescents and 9% per subclinical infection. This contrasts with a recurrence rate of 2.4% per patient and 17.5% per subclinical infection in a concomitant study of children receiving prophylaxis. There was therefore a downward trend with age, both in the incidence of haemolytic streptococcal infections and in the frequency with which these were followed by rheumatic fever. C. Bruce Perry

CHRONIC RHEUMATISM

336. Latex Particle Slide Tests in Rheumatoid Arthritis. Comparative Study

J. J. LANE JR. and J. L. DECKER. *Journal of the American Medical Association* [J. Amer. med. Ass.] 173, 982-985, July 2, 1960. 17 refs.

In this study reported from University of Washington School of Medicine, Seattle, the results of two rapid latex-particle slide tests used in rheumatoid arthritis, namely, the R.A. test and the eosin slide test, were compared with those of the latex fixation test, in which agglutination at a dilution of 1:160 or greater was regarded as positive. The eosin slide test was performed by adding 2 drops of stock latex suspension to a well-mixed drop containing serum and a 1% aqueous eosin solution. A positive result for agglutination produced a stippled granular appearance within 3 minutes. The R.A. slide test involved mixing a drop of the reagent with a drop of test serum diluted to 1:20 with glycine-saline buffer solution. The conversion of the cloudy suspension to a clear solution containing clumps was taken as a positive result.

Sera from 309 cases were examined by all three methods and 65 cases of classic rheumatoid arthritis showed positive reactions in 53, 57, and 58 cases respectively in the three tests outlined above. Rheumatoid arthritis with psoriasis was associated with a lack of agglutinating activity. In 10 out of 25 cases of gouty arthritis there were positive reactions with the slide tests, but only one was positive with the standard latex fixation test. Of 55 cases selected as likely to enhance false positive reactions and consisting of diffuse neoplasia and hyperglobulinaemic conditions, about one-third gave agglutination. The two slide tests were found to be more sensitive, but less specific, than the standard latex fixation test. All the positive results in the standard latex fixation tests were associated with positive results in the slide tests. Hyperglobulinaemia appeared to enhance the number of positive findings in the standard latex fixation test, but the increase in false positive reactions with the slide tests cannot be ascribed to non-specific hyperglobulinaemia. It is concluded that the slide tests are satisfactorily practical, and provide a quick method for use in the consulting room.

Harry Coke

337. Circulating Antibody Production in Rheumatoid Arthritis

R. GREENWOOD and M. BARR. *Annals of Physical Medicine* [Ann. phys. Med.] 5, 258-265, Aug., 1960. 2 figs., 13 refs.

An investigation of the antibody response in rheumatoid arthritis to primary immunization with tetanus toxoid is described in this paper from King's College

Hospital, London, and the Wellcome Research Laboratories, Beckenham, Kent. A group of 28 adult patients with active rheumatoid arthritis (diagnostic criteria of the American Rheumatism Association), who were receiving salicylates, hydroxychloroquine, and/or phenylbutazone, were given two injections of tetanus toxoid at 6 weeks' interval. Antibody production at the eighth week was compared by means of a mouse-protection test with that of a control group of 25 healthy subjects "matched for age and sex" [presumably 3 patients with rheumatoid arthritis had no paired control] and was found to be significantly greater; nevertheless in some of the rheumatoid patients the antibody response was poor. Since all the patients were receiving anti-rheumatic drugs, the authors studied the effect of these drugs on antibody production in guinea-pigs, relatively large doses being given. Both chloroquine and salicylate significantly reduced antibody production, but phenylbutazone had no such effect. In the patients with rheumatoid arthritis the antibody titre correlated with disease activity (modified Lansbury index) but not with the sensitized sheep-cell agglutination titre.

The authors briefly refer to the negative results obtained by others in studies of the antibody response in rheumatoid arthritis, and note that these were based on the effect of a booster dose of the antigen rather than on primary immunization. They suggest that the increased antibody response in rheumatoid arthritis may account for other serological abnormalities observed, such as increased streptococcal agglutinins. They mention certain further control studies that need to be carried out [and there are others, such as investigating the responses of sick controls and the question of protective factors other than specific antibody in the mouse-protection tests] before the effect they observed can be attributed to the rheumatoid arthritis in the patients in their series.

Allan St. J. Dixon

338. Rheumatoid Arthritis and Polyneuritis. (Polyarthrite rhumatoïde et multinévrite)

F. COSTE, F. DELBARRE, and F. BASSET. *Revue du rhumatisme et des maladies ostéo-articulaires* [Rev. Rhum.] 27, 169-177, June, 1960. 10 figs.

The authors point out that in their recent review, with Cayla (*Presse méd.*, 1959, 67, 1177; *Abstr. Wld Med.*, 1960, 27, 55) of 100 cases of rheumatoid arthritis treated for long periods with adrenocortical hormones it chanced that no case of polyneuritis occurred. However, they now comment on the increasing incidence of this complication and cite reports by various French workers, and in particular that by Johnson *et al.* (*Arthr. and Rheum.*, 1959, 2, 224; *Abstr. Wld Med.*, 1960, 27, 56) who described 17 cases, 3 in detail. In this paper from the Hôpital Cochin, Paris, they discuss the relationship between rheumatoid arthritis and periarteritis nodosa and describe 3 patients with long-standing rheumatic disease who developed signs suggesting involvement of several peripheral nerves and in each of whom biopsy specimens showed the histological appearances of periarteritis nodosa. In the first case the periarteritis appeared quite suddenly after several years of steroid therapy in rather high dosage. In the second, it occurred on the

abrupt withdrawal of corticotrophin (ACTH), and in the third, polyneuritis appeared in a patient who had previously exhibited toxic reactions to a variety of drugs. The change in the clinical picture, therefore, appeared to be related to the therapy. In 2 patients the condition markedly deteriorated and they subsequently died.

The authors conclude that although it is hazardous to discuss the relationship between rheumatoid disease and periarteritis nodosa, since the aetiology of both is so obscure, they consider nevertheless that periarteritis nodosa is a separate entity and suggest that it may occur in association with rheumatoid disease because the vascular changes which take place in the latter condition offer a milieu suitable for its appearance.

B. E. W. Mace

339. Clinical, Metabolic and Endocrinologic Effects of Abrupt Cessation of Maintenance Cortisone Acetate Therapy in Rheumatoid Arthritis

E. CALKINS, L. L. ENGEL, D. M. MITCHELL, P. CARTER, and W. BAUER. *Arthritis and Rheumatism* [Arthr. and Rheum.] 3, 204-217, June [received Aug.], 1960. 5 figs., 20 refs.

There is evidence that the abrupt cessation of corticosteroid therapy in patients with rheumatoid arthritis is followed by deterioration in the clinical condition and the appearance of symptoms resembling those of adrenal insufficiency. The authors of this paper from the Massachusetts General Hospital and Harvard Medical School, Boston, describe the immediate results of suddenly stopping cortisone treatment in 3 male patients with rheumatoid arthritis, all of whom had been receiving about 100 mg. of cortisone daily for at least 2½ years. Metabolic balance studies were carried out for a few days before cessation of treatment and for several days afterwards.

On the first day after cessation of cortisone administration, sodium retention continued; this was followed by sodium loss for a day or two, and then by sodium retention for several days. This accompanied an increase in plasma volume, while loss of sodium in sweat apparently ceased. Nitrogen, calcium, and phosphorus balances tended to change from negative to positive on stopping cortisone. Symptomatically, headache, anorexia, prostration, and muscular aching were attributed to cortisone withdrawal. Spontaneous improvement after 4 days was accompanied by the reappearance of cortisone metabolites in the urine, indicating a return of natural adrenal cortical activity. A relapse in the arthritic condition also began in all 3 cases within a day of cortisone withdrawal; joint swelling and stiffness increased, the erythrocyte sedimentation rate rose, and one patient became febrile, without clinical improvement at the 4th day. These symptoms are considered to explain the sodium retention and increased plasma volume which have previously been observed in active rheumatoid arthritis.

J. A. Cosh

340. Intra-articular Injections for Osteoarthritis

C. D. BONNER. *Rheumatism* [Rheumatism] 16, 84-89, Oct., 1960. 1 fig., 12 refs.

Neurology and Neurosurgery

341. The Convulsive Patterns Provoked by Indoklon, Metrazol and Electroshock: Some Depth Electrographic Observations in Human Patients

G. E. CHATRIAN and M. C. PETERSEN. *Electroencephalography and Clinical Neurophysiology* [Electroenceph. clin. Neurophysiol.] 12, 715-725, Aug., 1960. 7 figs., 31 refs.

In order to record convulsive patterns directly from the depths of the human brain multi-electrode leads were inserted through frontal burr holes into the brains of 5 schizophrenic patients at the Rochester State Hospital, Rochester, Minnesota, and left *in situ* for 24 to 72 days. The convulsions were induced by inhalation of 1 to 4 ml. hexafluorodiethyl ether in 2 of the patients and by injection of 10 to 15 ml. of a 10% solution of pentylene-tetrazol ("metrazol"; leptazol) in 3. In all 5 patients convulsions were also induced by electric shock.

Very clear recordings of brain potentials were obtained free from muscle artefact. With hexafluorodiethyl ether and metrazol prodromal discharges of random, asynchronous, irregular activity at 1.5 to 3 c.p.s. mixed with spikes occurred and were followed by a period of low-voltage discharge. Low-voltage fast activity then appeared, developing quickly into high-voltage rhythmic spikes at 10, slowing to 8, c.p.s. This discharge coincided with the tonic phase of the convulsion, but its development, voltage, form, and frequency varied from area to area. Coinciding with the clonic phase, the spike discharges became grouped and finally the discharge ceased, leaving the record quite flat for 10 to 90 seconds. Subsequently, high-voltage, generalized, irregular activity at 1 to 3 c.p.s. appeared, later being mixed with 5- to 7-c.p.s. waves. With electric shock, recording was not started for several seconds after the beginning of the tonic phase, but thereafter the discharges were similar.

The similarity of the prodromal features produced by hexafluorodiethyl ether and metrazol suggests that they act by a common mechanism.

L. G. Kiloh

342. Multiple Sclerosis in Twins and Their Relatives: Genetic Analysis of Family Histories. [In English]

N. C. MYRIANTHOPOULOS and R. P. MACKAY. *Acta genetica et statistica medica* [Acta genet. (Basel)] 10, 33-47, 1960. 12 refs.

The authors of this paper from the University of Minnesota, Minneapolis, and the University of Illinois College of Medicine, Chicago, report a genetic analysis of 1,112 relatives of 29 monozygotic and 25 dizygotic twin pairs, of whom at least one member of each pair suffered from disseminated sclerosis. The details of the survey from which these families were drawn were previously reported by the authors (*Arch. Neurol. Psychiat.*, 1958, 80, 667; *Abstr. Wild Med.*, 1959, 25, 362). It was found that the concordance rate between mono- and di-zygotic twins was not significantly different. On the other hand, the

incidence of disseminated sclerosis among the relatives of propositi was significantly higher than that in the general population (1 in 2,000). Thus, in the siblings of propositi it was 49 to 117 times higher according to the strictness of the diagnostic criteria; in the parents and the children of propositi it was 32 and 35 times higher, respectively, than in the general population.

After formal genetic analysis of these findings the authors conclude that "it seems reasonable to accept that genetic factors of considerable magnitude operate in the etiology of multiple sclerosis—most likely a pair of autosomal recessive genes—but these are subject to powerful environmental influences which, in fact, have the upper hand". They admit, however, that there may be other explanations for the data. Discussing briefly the likely environmental factors they suggest that climate must certainly have some effect in influencing the penetrance of genetic factors.

J. B. Cavanagh

343. Acute Radiculoneuritis. Syndrome of Guillain-Barré or Landry's Syndrome? (Les ganglio-radiculo-névrites aiguës. Syndrome de Guillain-Barré ou syndrome de Landry?)

P. VAN GEUCHTEN and C. LATERRÉ. *Revue neurologique* [Rev. neurol.] 102, 201-219, March [received Sept.], 1960. 17 figs., 11 refs.

Considerable difference of opinion exists as to whether the Guillain-Barré syndrome, typified by flaccid paralysis and albumino-cytologic dissociation in the cerebrospinal fluid (C.S.F.), and an acute febrile polyneuritis developing into a Landry's paralysis are separate conditions or the same. The authors writing from the Institute of Neurology, Louvain, describe the clinical and histopathological findings in 8 cases, in 3 of which there was a typical history of Landry's paralysis and all of which ended fatally. The first case ran a subacute course of 6 days and showed only a slight increase in protein in the C.S.F. The other 2 cases were less acute, the courses being 17 days and about 4 weeks respectively, and showed an albumino-cytologic dissociation in the C.S.F., as in the Guillain-Barré syndrome. In all 3 cases the cord was almost intact. Inflammatory reaction in the nerve roots and their ganglia was only slight in the first case, but more marked in the other 2. The axons showed myelin degeneration and Schwann-cell reaction. The ganglion cells were moderately changed. Death was due to respiratory trouble and difficulty in swallowing.

In the other 5 cases in which there was ascending flaccid paralysis tracheotomy was carried out; 3 patients recovered completely but 2 died of cardiac failure, although improvement in the neurological state was occurring. Both these fatal cases showed histological changes similar to those seen in the previous 3. In 3 cases there was an albumino-cytologic dissociation in the C.S.F., and in one sensation was affected. The rapidly

ascending flaccid paralysis in these cases suggested the diagnosis of Landry's paralysis, while the C.S.F. changes were suggestive of the Guillain-Barré syndrome. The authors discuss at length the clinical and histological similarities and differences of the two conditions and the possibility of distinguishing between them. They conclude that it may be impossible to define exactly the Guillain-Barré syndrome. [This part of the paper is impossible to abstract and should be read in full by those interested.] The authors state that they will continue to designate as examples of the Guillain-Barré syndrome those cases showing peripheral motor disturbance with or without sensory troubles and accompanied by raised C.S.F. albumin content and to include among these certain cases showing an ascending flaccid paralysis with increased C.S.F. protein content.

R. Wyburn-Mason

BRAIN AND MENINGES

344. Post-traumatic Obstruction of the Aqueduct of Sylvius and Postdecompression Cerebral Edema Treated by Ventriculostomy

R. FORD and E. L. SPATZ. *New England Journal of Medicine* [New Engl. J. Med.] 263, 263-267, Aug. 11, 1960. 11 figs., 6 refs.

The problem presented by acute brain swelling after the removal of a space-occupying lesion following head injury is discussed in this paper from Harvard Medical School, Boston.

The underlying pathology of the phenomenon is outlined and the importance of aqueduct obstruction consequent upon the compression and angulation caused by the tentorial pressure cone is stressed. The acute internal hydrocephalus so induced is considered to be an important factor in the production of the swollen brain—that is, the volume of cerebrospinal fluid trapped above the kinked and obstructed aqueduct increases the intracranial tension directly. In the authors' view the relief of this acute internal hydrocephalus by transfrontal ventriculostomy is an essential preliminary to any direct operative intervention and postoperative ventricular catheter drainage will obviate any tendency towards recurrence.

The procedure, with 11 illustrations which lend support to this thesis, is described in detail. J. B. Foster

345. High Blood-pressure and Stroke. Necropsy Study of Heart-weight and Left Ventricular Hypertrophy

C. J. DICKINSON and A. D. THOMSON. *Lancet* [Lancet] 2, 342-345, Aug. 13, 1960. 3 figs., 5 refs.

The authors have previously shown that narrowing of the vertebral artery is more closely associated with hypertension than is narrowing of the internal carotid artery, and further, that in patients who die from stroke a reduction in the fluid carrying capacity of the main cerebral arteries is seen at necropsy, this being observed in cases of cerebral haemorrhage as well as in those of cerebral softening and infarction. These findings appear to indicate that strokes in the vertebral artery territory should be associated with a slightly higher blood pressure

than those in the internal carotid artery territory and that high blood pressure should be as closely associated with cerebral softening and infarction as it is with haemorrhage.

At the Middlesex Hospital, London, the necropsy records for the years 1931-59 of all cases of brain damage were examined, excluding cases of malignant hypertension, trauma, cerebral tumour, cerebral aneurysm, bleeding diathesis, and presumed embolism. Thus, only cases in which death was due to vascular disease or hypertension were studied. The heart weight, which was noted for each case, provided evidence, or otherwise, of hypertension. A total of 335 records were examined, and it was found that in those cases in which hindbrain stroke (vertebral artery area) had occurred the heart weight was greater than in those in which there had been a forebrain stroke (internal carotid area). The mean heart weight in cases of cerebral haemorrhage did not differ significantly from that in cases of cerebral infarction.

The authors consider that these findings support the contention that narrowing of the main cerebral arteries, especially the vertebral arteries in their cervical course, "has a primary causal role in benign 'essential' hypertension" and that cerebral haemorrhage and cerebral infarction both have the same cause.

G. S. Crockett

346. Metastatic Tumors of the Brain. A Follow-up Study of 195 Patients with Neurosurgical Considerations

M. D. SIMIONESCU. *Journal of Neurosurgery* [J. Neurosurg.] 17, 361-373, May [received July], 1960. 4 figs., 37 refs.

An analysis is presented of a series of 195 patients with verified cerebral metastases admitted to State Hospital No. 9, Bucharest, between 1955 and 1959, representing 6.7% of a total of 2,901 patients with intracranial space-occupying lesions. It is pointed out that there were 980 cases of cerebral gliomata in the series so that the comparative frequency of cerebral metastases was 1 in 5. The peak age incidence was in the age group 40 to 60 years, with extremes of 18 and 80 years; the condition was more often seen in males than in females, owing it is stated to the "higher frequency of metastases of pulmonary origin in males".

The site of the primary tumour was the lung in 38% of cases, breast in 22%, skin in 6%, digestive tract in 3%, thyroid gland in 2%, and other sites in 1% or less; in 11% of cases the site was unknown. The duration of symptoms was less than 3 months in 62% and over one year in 6%. In 109 (56%) of the cases the cerebral lesion was solitary [no analysis of the primary sites of these is given]. In 64% of the cases of tumour of the lung, but rarely in other cases, the primary lesion was not detected before the patient was admitted to hospital, emphasizing that metastases to the central nervous system occur from bronchial carcinoma before the lung tumour is clinically or even radiologically apparent. Another important feature was the interval between removal of a primary cancer and onset of cerebral symptoms, this being over 2 years in 70% of cases of carcinoma of the breast, under one year in 75% of cases of carcinoma of the bronchus, 5 years in one case of

digestive-tract carcinoma, and 6 years in one of renal carcinoma. There were associated general signs of cachexia, with a loss of body weight exceeding 10 kg., in 12% of the cases. The initial neurological symptoms were psychic disorders in 18%, raised intracranial pressure in 24%, and focal neurological disturbances in 30%.

The most conclusive neuroradiological investigation carried out was ventriculography, but the author points out that the cerebral oedema which is associated with metastatic lesions may give misleading results, as it did in 6 (4.75%) of 126 cases in this series. Of the 195 patients 23 were not operated on and 19 of these died within 6 months. Of 172 patients subjected to operation 66 (38%) died within 3 weeks, and 89 (51%) showed evidence of recurrence within 6 months of operation. However, 4 patients survived and were apparently well for one to 6½ years, including one patient with bronchogenic metastases who survived 6½ years.

The author considers that although the results of surgery are discouraging, operation is justified because a few patients may be rendered symptom-free for several years. In addition, in many patients with a solitary metastasis the symptoms of intracranial hypertension are so severe that some form of palliative surgery is imperative.

J. V. Crawford

347. A Survey of the Epilepsies in General Practice

A REPORT BY THE RESEARCH COMMITTEE OF THE COLLEGE OF GENERAL PRACTITIONERS. *British Medical Journal* [Brit. med. J.] 2, 416-422, Aug. 6, 1960. 5 figs., 8 refs.

A survey of epilepsy as seen in 67 general practices in England and Wales (population at risk 288,830) was carried out between October, 1957, and September, 1958. The over-all incidence of chronic epilepsy was 4.19 per 1,000 population, with a slight preponderance in males; first seizures occurred in 0.63 per 1,000. The findings are analysed by age and sex of the patients, the nature of the fits, the response to treatment, and the employability of the patients. Major epilepsy accounted for four-fifths of all cases. The sex incidence of epilepsy was approximately equal except for a preponderance of males in the age group 10 to 14 years and again in old age. The incidence among school-children of 4 per 1,000 was higher than expected. First fits occurred mainly in the age group 0 to 4 years, the incidence being 3.55 per 1,000, as compared with a range of 0.15 to 0.85 per 1,000 in the older age groups. Social problems were present in 17% of cases. Analysis of the results of drug therapy showed that seizures were controlled in 44% of patients with grand mal epilepsy, but only in 32.4% of patients with other types of epilepsy. Phenytoin was 2½ times more popular with general practitioners than phenytoin sodium. In 18% of the practices (population 60,000) no first fit was recorded in the survey year; it would thus appear that not all patients seek advice at the time of the first seizure. The authors state that about 5% of subjects have a seizure of some kind during life and that approximately one in 8 of those having a first fit will become chronic epileptics and one in 160 will be disabled and unemployable.

William Hughes

SPINAL CORD

348. A Cutaneous Disorder of Connective Tissue in Amyotrophic Lateral Sclerosis: a Histochemical Study H. M. FULLMER, H. D. SIEDLER, R. S. KROOTH, and L. T. KURLAND. *Neurology* [Neurology (Minneapolis)] 10, 717-724, Aug., 1960. 13 figs., 9 refs.

The authors of this paper from the National Institutes of Health, Bethesda, describe changes occurring in the connective tissue of the dermis in patients suffering from amyotrophic lateral sclerosis which they believe to be of significance in this disease. They claim that slightly more than half the biopsy specimens of abdominal skin showed excessive amounts of mucopolysaccharide, elastosis, an ill-defined degenerative change in the arrectores pilorum, and focal changes in the staining affinities of the dermal collagen. Only histochemical methods were used to demonstrate these changes, for which no adequate explanation could be found. It is suggested, however, that examination of skin biopsy specimens for these features may be helpful in diagnosis.

J. B. Cavanagh

349. Intradural Racemose Angioma of the Spinal Cord. (Les angiomes racémeux intraduraux de la moelle épinière)

H. VERBIEST and L. CALLIAUW. *Revue neurologique* [Rev. neurol.] 102, 230-243, March [received Sept.], 1960. 3 figs., 27 refs.

The authors briefly review the world literature on the pathological classification of intradural vascular tumours and malformations of the spinal cord and stress the difficulty of making a preoperative diagnosis. They confine their observations to and give typical histories of 13 cases of vascular malformations, verified at operation, occurring in 11 male and 2 female patients; 2 of the former were boys aged 6 and 10 years at the time of operation, the others ranging in age from 34 to 70 years. In 8 cases the lesions were those of a racemose venous angioma, 6 being situated at the lower end of the cord, one at the level of D 5-6, and one at D 7-8. In 2 other cases in which the lower end of the cord was involved the lesions were thought to be arterio-venous angiomas. In 3 cases the lesions were considered to be arterial angiomas, these being situated at the lower end of the cord, at C 5, and at D 6-8 respectively.

The authors then analyse the age incidence of symptoms of the reported cases of venous and arterial angiomas. In both types the maximum incidence is between 20 and 70 years. They stress the rarity of symptoms in children and confirm the regional distribution of the various types of lesion, as described by previous authors. In their own series 2 cases presented with spinal subarachnoid haemorrhage, but the other 11 showed the classic slow evolution punctuated by apoplectic episodes. The cerebrospinal fluid and myelographic changes are described and various views on aetiology and prognosis are discussed. While most surgeons adopt a conservative attitude in treatment and limit themselves to dural decompression, the authors in most cases practised coagulation of the vessels, with varying success.

R. Wyburn-Mason

Psychiatry

350. Homosexuality and Heterosexuality in Identical Twins

J. D. RAINER, A. MESNIKOFF, L. C. KOLB, and A. CARR. *Psychosomatic Medicine [Psychosom. Med.]* 22, 251-258, July-Aug., 1960. 15 refs.

The authors of this paper from the New York State Psychiatric Institute and the Department of Psychiatry, College of Physicians and Surgeons, New York, describe a study of the divergent sexual orientation in two sets of identical twins. The approach represented a variation of the classic use of twin studies in that an attempt was made to discover explanations for dissimilarities rather than similarities in uni-ovular twins. It is pointed out that different behavioural patterns in such twins must be related to post-natal experience.

The first set of twins were female schizophrenic subjects and the second were male psychoneurotic subjects. In each pair one member was heterosexual and the other homosexual. The subjects were studied by means of a free association technique, supplemented by physical, biochemical, and psychological examinations and by a study of family and social environment.

In the schizophrenic twins the sexual roles did not achieve genital expression and their investigation served as a preliminary to that of the psychoneurotic pair in whom the sexual differentiation existed at a genital level. Although the homosexual member of the second set of twins was less intensively studied than his heterosexual brother, it came to light that because of a slight anatomical distinguishing feature the mother had developed a special attachment to the former; the heterosexual twin was named in accordance with the father's wishes and was rejected by the mother. Both twins had been homosexually seduced; therefore, such seduction was not considered a sexual determinant. Analysis of the steroid content of the urine disclosed similar patterns in these male twins and nuclear sexing techniques indicated that both had a male chromatin pattern.

It is concluded that the divergent sexual orientation may be reasonably explained on the basis of the early parent-child relationship.

A. Balfour Sclare

351. False Pregnancy in a Male

J. A. KNIGHT. *Psychosomatic Medicine [Psychosom. Med.]* 22, 260-266, July-Aug., 1960. 4 refs.

A clinical study of a case of pseudo-pregnancy in a male is reported. The process of psychoanalytically orientated psychotherapy itself constituted a means of investigation as well as of treatment. A 33-year-old unmarried merchant seaman complained of abdominal distension, morning nausea, and bulimia shortly after a shipmate began to talk of getting married and having a child. He believed that by virtue of a miracle he had become pregnant. Apart from the delusion that he represented a woman in a man's body he was fairly

rational. Early paranoid schizophrenia was provisionally diagnosed. A study of the patient's history disclosed that he had no memory of his mother and that he had felt rejected by a series of foster-mothers as well as by his father. He had always experienced a deep sense of insecurity concerning his identity, and he had had both heterosexual and homosexual experiences. The nuclear problem, however, was considered to be one of homosexuality in which a strong dependency component was implicit. After 2 months of analytic psychotherapy the gastro-intestinal symptoms began to subside. Within 4 months he was virtually symptom-free and had acquired considerable insight into his frustrations and needs and some understanding of the relationship of emotions to bodily functions.

A. Balfour Sclare

352. A Comparison of Psychological Characteristics and Physiological Reactivity in Ulcer and Rheumatoid Arthritis Groups. I. Psychological Measures

S. E. CLEVELAND and S. FISHER. *Psychosomatic Medicine [Psychosom. Med.]* 22, 283-289, July-Aug., 1960. 6 refs.

The authors have already described a set pattern of behavioural activity in patients with rheumatoid arthritis (*Psychosom. Med.*, 1954, 16, 327). At the Veterans Administration Hospital, Houston, Texas, this work on the psychological characteristics of such patients has been repeated and extended. It had previously been found that patients with rheumatoid arthritis have fantasies of a well defined body-image boundary, reflected in a high "barrier score" on psychological testing, and that in contrast, patients with peptic ulcer have low scores on the barrier scale but have a high "penetration score", reflecting a weak and poorly defined body-image boundary.

In the present investigation 26 male patients with rheumatoid arthritis and 33 similar patients with peptic ulcer were subjected to a standard interview and the Holtzman ink-blot test (Form B), the interview being directed towards certain limited areas of personality function, for example, participation in athletic and domestic activities and mode of arousal of aggressive feelings. The Holtzman ink-blot test was chosen as being more appropriate than the Rorschach test for such an investigation. In general the results of the previous study were confirmed. Patients with rheumatoid arthritis showed a significantly high degree of participation in sports activities before the onset of the illness. The findings indicated that arthritic patients are intolerant of exhibitionistic behaviour in others because of their own inner, aggressive, exhibitionistic impulses. The results of the ink-blot test confirmed that patients with rheumatoid arthritis have a concept of their body image in terms of a well marked boundary, whereas patients with peptic ulcer regard the body image as being characterized

by a vulnerable interior. In each group a pronounced hostile affect was noted; in the rheumatoid group this affect was expressed in terms of athleticism before the onset of the illness, whereas in the ulcer group hostility was experienced as a near-paranoid sense of deprivation by the environment.

A. Balfour Sclaire

353. A Comparison of Psychological Characteristics and Physiological Reactivity in Ulcer and Rheumatoid Arthritis Groups. II. Differences in Physiological Reactivity

S. FISHER and S. E. CLEVELAND. *Psychosomatic Medicine* [Psychosom. Med.] 22, 290-293, July-Aug., 1960. 3 refs.

In this further study [see Abstract 352] the authors examined the hypothesis that subjects with well defined body-image boundaries are inclined to channel autonomic excitation via the external body layers and that those with indefinite boundaries display an opposite physiological pattern. Rheumatoid arthritis was chosen as a disease affecting the outer body layers and peptic ulcer as an example of an internal psychosomatic disorder.

In 26 male patients with rheumatoid arthritis and 34 similar patients with peptic ulcer external reactivity was measured by means of the galvanic skin reflex (G.S.R.), and internal reactivity by the heart rate recorded on an electrocardiograph. Simultaneous polygraphic recordings of G.S.R. and heart rate were made under two different sets of conditions: (1) during an 80-second period of "stress" immediately after the crash of a heavy iron bar falling to the floor, and (2) during a subsequent 80-second period of relaxation. The results indicated that under stressful conditions the rheumatoid patients manifested greater G.S.R. than heart-rate activity, while in the ulcer patients the reaction was the opposite, the original hypothesis being thus confirmed. It was noted that during the period of relaxation there was no significant physiological difference between the 2 groups. This supplementary physiological test would seem to show that when psychosomatic symptoms are induced by stress the patient's previously established tendencies to channel external versus internal responses are likely to be a determinant of the choice of type and site of symptoms.

A. Balfour Sclaire

354. Some Personality Characteristics of Asthmatic Children

T. ALCOCK. *British Journal of Medical Psychology* [Brit. J. med. Psychol.] 33, 133-141, 1960. 13 refs.

At the Tavistock Institute of Human Relations, London, a psychological investigation of a group of asthmatic children was carried out, employing the Rorschach test to assess personality, the aim of the study being to discover whether the asthmatic subjects displayed any characteristic features which were not evident in non-asthmatic children.

The experimental group consisted of 25 asthmatic children between the ages of 7 and 11 years, while the control groups consisted of 25 normal children, 25 patients from a child-guidance clinic, and 25 children suffering from various chronic physical disorders (ex-

cluding asthma). The latter groups were matched with the experimental group for age, sex, intelligence, educational status, and socio-cultural background. In the Rorschach test 9 items were added to the conventional indices, and the findings were assessed by an independent statistician.

The results showed that the asthmatic children differed significantly from the normal group on 14 indices, from the clinic cases on 12, and from the physically ill group on 10. The Rorschach records of the asthmatic children showed that they imposed considerable restraint upon all living objects, and it is inferred that "the asthmatic seems to be sitting on the safety valve of his emotions". One interesting feature in the group of children with chronic organic disorders was a poverty of mother-figures in their responses. A deep and pervasive depressive feeling-tone was noted among the asthmatic subjects, who seemed to display a high degree of emotional tension which was not appropriately released.

[The author claims that the above-mentioned depressive features in asthmatic patients have not previously been emphasized in the literature; but see Knapp and Nemetz, *Psychosom. Med.*, 1957, 19, 466; *Abstr. Wld Med.*, 1958, 23, 420.]

A. Balfour Sclaire

355. Reading, Reckoning, and Special Schooling among the Mentally Handicapped

Z. STEIN, M. SUSSER, and E. A. LUNZER. *Lancet* [Lancet] 2, 305-307, Aug. 6, 1960. 7 refs.

There has been a dearth of follow-up information about the benefit which the mentally handicapped child derives from special school education. This paper from the Departments of Education and of Social Medicine, Manchester University, analyses the end-result of different educational programmes in 49 educationally-subnormal men and women, aged 20 to 24 years, who were divided into two groups according to whether they had attended ordinary or special schools. Of 31 who had attended ordinary schools 10 were illiterate, but of the 18 who had been to special schools only one was illiterate, this difference being statistically significant at the 5% level; "illiteracy" was defined as a reading age of under 7 years on the Schonell reading test. The mean I.Q. (on the Stanford-Binet scale) was 66 (S.D. 9) for the special-school group and 70 (S.D. 10) for the ordinary-school series. Of 14 with an I.Q. of under 70 who had attended ordinary school 8 were illiterate, but all of 10 with a similar I.Q. who had been to a special school could read, although half were "semi-illiterate" (reading age 7 to 9 years). Of the 17 ordinary school pupils with an I.Q. of 70 or over, 2 were illiterate, and of 8 similar special-school pupils one was illiterate. The presence of clinical abnormality in 20 individuals (13 with neurological signs, 4 imbeciles, and 3 with severe hearing defects) did not influence the effects of special schooling, only one out of 9 such subjects remaining illiterate, compared with 4 out of 11 who attended ordinary schools. As the patients were tested several years after leaving school and some had learned to read after schooling had stopped, the suggestion is made that reading lessons for older patients in occupation centres

and mental deficiency hospitals may be worth while. In regard to "reckoning", ordinary school education had left 7 subjects "innumerate", whereas 4 who had attended special schools remained innumerate (score less than 4 on the Wechsler adult intelligence scale, arithmetic sub-test). Of 23 with an I.Q. over 65 (Stanford-Binet) who had attended ordinary schools 5 were innumerate, but none of 10 taught at special schools scored less than 4.

It is pointed out that the subjects of this study had been to different special schools and had thus been taught by different teachers and methods, but nevertheless a common factor was the small number of children in each class which permitted much more concentration on the individual child. No evidence was obtained to show whether the greater improvement taking place in the special-school pupil was due to segregation or to teaching methods, but it was shown that such improvement was not related to clinical condition or family background.

[Reading classes have been held in mental deficiency hospitals for many years (see Rudolf, *Brently Colony Reports*, 1933).]

G. de M. Rudolf

SCHIZOPHRENIA

356. Treatment of Schizophrenic Reactions with Phenothiazine Derivatives. A Comparative Study of Chlorpromazine, Trifluorpromazine, Mepazine, Prochlorperazine, Perphenazine, and Phenobarbital

J. F. CASEY, J. J. LASKY, C. J. KLETT, and L. E. HOLLISTER. *American Journal of Psychiatry* [Amer. J. Psychiat.] 117, 97-105, Aug., 1960. 2 figs., 21 refs.

A total of 640 newly-admitted schizophrenic men in 35 VA [Veterans Administration] hospitals were randomly assigned to chlorpromazine, trifluorpromazine [trifluorpromazine], mepazine, prochlorperazine, perphenazine, and phenobarbital groups. Treatment followed a double-blind procedure for 12 weeks. Patients were started on low "equivalent" doses of each drug which were gradually increased in a predetermined manner during the first 4 weeks. During the final 8 weeks, each prescribing physician adjusted the dose for each of his patients in order to evoke an optimal therapeutic response.

Average daily doses during the flexible period were: chlorpromazine, 635 mg.; trifluorpromazine, 175 mg.; mepazine, 190 mg.; prochlorperazine, 90 mg.; and perphenazine, 50 mg. Clinical evaluations using two rating scales provided 24 criteria of change. For each criterion, the mean of each of the 6 treatment groups adjusted for the net effect of 12 control variables was compared by analysis of multiple covariance with the mean of every other treatment group at each of three evaluation periods; first month, the following 2 months, and over the entire 3 months. Side effects, hematologic and hepatic function data were also recorded during the course of treatment. One hundred and sixty-eight patients failed to complete the study.

In general, the results indicated that all 5 phenothiazine derivatives were therapeutically more effective than

phenobarbital. Mepazine was less effective than the other 4 drugs at the doses employed. No significant differences in therapeutic efficacy were noted between chlorpromazine, trifluorpromazine, prochlorperazine, and perphenazine. Criterion measures showing change toward improvement after treatment with phenothiazine derivatives included resistiveness, belligerence, thinking disturbance, and degree of illness. Other criteria affected favorably, especially by the 4 more potent phenothiazines, were motor disturbance, paranoid projection, perceptual distortion and withdrawal.

Only 21 patients (3%) were discontinued from treatment because of side reactions or deviant laboratory tests. Most side reactions, especially the extrapyramidal syndromes, were produced by perphenazine and prochlorperazine. Phenobarbital was associated with a number of side reactions ("turbulence", autonomic symptoms) commonly attributed only to the phenothiazine derivatives. Abnormal hematologic tests including eosinophilia, leucocytosis, and leucopenia were neither frequent nor severe. The distribution of the 36 patients with leucopenia was not significantly different among the treatment groups. Continued treatment with the drugs in 31 leucopenic patients produced no case of agranulocytosis. Although abnormal hepatic tests occurred in 88 patients, these were sporadic. No clear-cut case of jaundice or hepatic dysfunction was encountered during treatment.—[Authors' summary.]

357. Nuclear Sex and Body-build in Schizophrenia

V. COWIE, A. COPPEN, and P. NORMAN. *British Medical Journal* [Brit. med. J.] 2, 431-433, Aug. 6, 1960. 1 fig., 10 refs.

Recent surveys have shown that the androgyny score [$3 \times \text{bi-acromial diameter (cm.)} - 1 \times \text{bi-iliac diameter (cm.)}$] is significantly reduced in schizophrenic patients. There is also some evidence that anomalies of nuclear sex are associated with reductions in the androgyny score and with certain mental abnormalities, such as intellectual deficiency, or such symptoms as apathy and shyness in patients with Klinefelter's syndrome. The authors inferred from these findings that there may be some schizophrenics showing both a low androgyny score and changes in nuclear sex. They therefore studied 100 male and 100 female patients in whom schizophrenia had been diagnosed, and found that the average androgyny score in male patients was only 86.2 (normal, 90.1) and in female patients only 76.1 (normal, 78.9). They then selected for nuclear sexing 6 male patients with a normal androgyny score, 16 males with scores of less than 82, and 20 females with scores of less than 72. No anomalies of nuclear sex were found in any of the schizophrenic patients with low androgyny scores, thus disproving the hypothesis that schizophrenic symptoms and changes in body build could be associated with anomalies of nuclear sex.

F. K. Taylor

358. Human Ecology, Disease, and Schizophrenia

L. F. CHAPMAN, L. E. HINKLE JR., and H. G. WOLFF. *American Journal of Psychiatry* [Amer. J. Psychiat.] 117, 193-204, Sept., 1960. Bibliography.

Paediatrics

PREMATURITY AND NEONATAL DISORDERS

359. Causes of Death in Premature Infants. [In English]

A. SKOGRAND and K. HARNAES. *Acta pathologica et microbiologica Scandinavica* [Acta path. microbiol. scand.] 49, 321-328, 1960. 1 fig., 32 refs.

Of 536 premature infants seen at the Children's Hospital, Oslo, during the 4 year-period 1954-7 a total of 120 died, the majority within 2 days of birth. Analysis of these 120 cases showed that mortality was highest in infants with the lowest birth weight. Hyaline membrane was the commonest cause of death in the series (43 cases) and the commonest cause of death, usually in the first and second days of life, in infants weighing 1,000 to 2,000 g. at birth. Intracranial haemorrhage accounted for death in 22 infants, in 14 of whom the bleeding was intraventricular; other causes were atelectasis in 22 cases, pneumonia in 14, pulmonary haemorrhage in 9, and kernicterus, unassociated with Rh or ABO incompatibility, in 5. In the remaining 5, death was due respectively to oesophageal atresia, congenital cardiac defect, volvulus, hydrops foetalis, and intestinal perforation. [In general, these findings reflect the experience of most neonatal units.] R. M. Todd

360. Lability of Vasomotor Reactions as an Index of the Severity of Intracranial Damage in the Newborn. (Лабильность сосудистых реакций как показатель глубины патологического состояния при внутричерепной травме новорожденных)

JU. F. ZMANOVSKI and V. N. ŠIŠKOVA. *Вопросы Охраны Материнства и Детства* [Vop. Ohrany Materin. Dets.] 5, 59-54, July-Aug., 1960. 4 figs.

Vasomotor reactions to cold were studied by means of an electrical-resistance thermometer in 80 newborn babies of whom 50 had suffered intracranial birth injury. The basal temperature of a skin segment was first determined and then a test-tube containing melting ice was applied for 10 seconds and the skin temperature again recorded at various intervals thereafter; the findings are presented graphically. In healthy infants the initial fall in temperature varied from 1 to 1.2° C. and the original normal temperature was restored in 1½ to 2 minutes. In 14 infants with mild or moderate intracranial injury the initial temperature of 32.2° C. was reduced by over 2° C. and did not return to normal until after 4 minutes. In 16 infants with severe head injury at birth the mean initial temperature was 34.4° C., the average fall was over 3° C., and recovery took 6 to 8 minutes or more.

In the second series of experiments the dynamics of the regional vasomotor reactions were studied during the first 9 days of life in 10 healthy infants and 20 babies with intracranial birth injury. In healthy babies the extent of the fall in temperature is small and the recovery

stage is gradually shortened to under 1½ minute. In infants with birth injury the vasomotor reactions remain labile, this lability lessening with clinical improvement. If the injury is slight and recovery complete by the 9th day the reactions become analogous to those of healthy infants. If the injury is more severe, however, the process of clinical recovery and the labile vasomotor reactions may be extended over a longer period of time.

S. W. Waydenfeld

361. Prospective Experience with Maternal Rubella and the Associated Congenital Malformations

R. H. MICHAELS and G. W. MELLIN. *Pediatrics* [Pediatrics] 26, 200-209, Aug., 1960. 33 refs.

The association between rubella in pregnancy and congenital malformations in the infant was studied in 25 mothers who contracted rubella during pregnancy and in 95 others who were exposed to infection during pregnancy, all the patients being seen at the Sloane Hospital for Women, New York, between 1946 and 1959. In 15 of the 25 patients who had rubella the infection occurred before the 16th week of pregnancy and 8 of these had normal live-born infants; in 4 cases pregnancy terminated in spontaneous abortion and in 3 cardiac abnormalities were noted in the infants after birth.

Of the 95 patients who were exposed to infection but did not have a clinical attack 81 had normal infants. There was abortion or stillbirth in 6 cases in this group while in 8 the infants were malformed, the malformations including anencephaly in 2, hypospadias in 2, and tracheo-oesophageal fistula in one.

The authors reviewed the literature on the incidence of malformations in infants following rubella in pregnancy and found that when rubella was contracted during the first month the infant was malformed in 47% of cases, the comparable figure for the second month being 22%, for the third month 7%, and for the fourth month 6%.

John Fry

362. Diagnosis of Neonatal Jaundice by Patterns of Serum Transaminase

S. KOVE, R. PERRY, and F. WROBLEWSKI. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] 100, 47-68, July, 1960. 13 figs., 36 refs.

From the New York University College of Medicine the authors describe the pattern of change in serum transaminase values in a number of jaundiced newborn infants. It is already known that the levels of glutamic oxalacetic transaminase (G.O.T.) and glutamic pyruvic transaminase (G.P.T.) are higher in the first 2 months of life than subsequently. These enzymes, which are widely distributed in the body, are particularly active in the liver and hence during hepatocellular destruction they are liberated and give rise to increased levels in the serum. Previous reports, amplified by the results recorded in this paper, showed the value of serial measurements of serum transaminase activity in the differential

diagnosis of neonatal jaundice and in the selection of infants with obstructive jaundice for laparotomy.

Normal values were found in physiological jaundice (even when protracted), in jaundice caused by absorption from an encapsulated haematoma, and in that associated with kernicterus. The values were also normal in haemolytic jaundice, with the exception of a transient and small rise in one severe case reported here. In obstructive jaundice, whether due to malformation of the bile ducts or to the "inspissated bile syndrome", the level rose slowly, usually remaining below 800 units per ml. Viral hepatitis was associated with an early and rapid rise, the result usually exceeding 800 units per ml. In one case of cytomegalic inclusion disease the serum G.O.T. activity was 295 units per ml. on the second day of life and death occurred on the 7th day. The authors emphasize the value of a series of estimations rather than a single one, and stress the importance of taking the first sample of blood early.

[The detailed case histories and charts are of interest.]

F. P. Hudson

363. Surgical Exploration in Obstructive Jaundice of Infancy

T. V. SANTULLI, R. C. HARRIS, and K. REEMTSMA. *Pediatrics* [Pediatrics] 26, 27-35, July, 1960. 5 figs., 25 refs.

From a review of 71 cases and an evaluation of frozen-section examinations of liver biopsies, the authors propose the following method of management of infants with prolonged obstructive jaundice.

All patients are carefully selected on the basis of history, clinical findings and appropriate laboratory investigation. Laboratory studies found to aid in the differential diagnosis are: serial determinations of bilirubin (conjugated and unconjugated) in the serum, zinc sulfate turbidity test, cholesterol and cholesterol esters in serum, estimation of bile pigment in urine and stool, studies of the maternal and infant blood factors and erythrocyte fragility. Determinations that have not been useful in the differential diagnosis are: cholesterol esterase, alkaline phosphatase and cephalin flocculation. The activity of transaminases in the serum may prove helpful and are currently under study. The measurement of the prothrombin time should be included in the preoperative studies.

If the diagnosis is impossible by the age of 7 weeks, then surgical exploration is carried out. This consists of exposing the liver, taking a biopsy for frozen-section examination and performing a cholangiogram, if possible. With increasing experience, confidence has been acquired in interpretation of the frozen-section of the liver biopsy at this age. The authors are convinced of its value in helping the surgeon establish the diagnosis before proceeding with further exploration of the bile ducts.

By this method of management, surgical exploration need not be delayed beyond 7 weeks of age. Thus a patient with congenital atresia of the bile ducts, who may be fortunate enough to have a correctable lesion, will not be deprived of the only possible chance of cure. At this age it is unlikely that biliary cirrhosis will have

progressed to a severe degree. Admittedly, it would be preferable to explore such a case earlier, but more experience is needed in diagnosis by frozen-section examination at an earlier age.

It does not appear that any patient with hepatitis or other non-surgical condition has been harmed either by the anesthesia or surgical trauma attendant on this limited procedure. One of the greatest advantages of the frozen-section examination has been the information provided to the surgeon at a crucial time during the exploration. With this information the surgeon should be able to avoid unnecessary exploration of the bile ducts and possible injury to patent ducts, as well as unnecessary biliary-intestinal anastomoses which have been performed in the past because of mistaken diagnoses.—[Authors' summary.]

CLINICAL PAEDIATRICS

364. Idiopathic Hypercalcemia of Infancy

D. O'BRIEN, T. D. PEPPERS, and H. K. SILVER. *Journal of the American Medical Association* [J. Amer. med. Ass.] 173, 1106-1110, July 9, 1960. 2 figs., 16 refs.

The complete biochemical findings in 4 infants with idiopathic hypercalcaemia who were treated by the administration of adrenocortical steroids and restriction of calcium and vitamin-D intake, are given in this report from the University of Colorado Medical Center, Denver. The authors present photographs to illustrate the diagnostic importance of the typical facies, which is stressed, and discuss the aetiology and biochemistry of the condition in detail.

Janet Q. Ballantine

365. Ulcerative Colitis in Childhood: a Study of Its Natural History

J. W. PLATT, B. E. SCHLESINGER, and P. F. BENSON. *Quarterly Journal of Medicine* [Quart. J. Med.] 29, 257-277, April [received Aug.], 1960. 1 fig., 28 refs.

The authors review a series of 62 cases of ulcerative colitis in childhood seen between 1938 and 1956 in private practice (5), at the Hospital for Sick Children, Great Ormond Street (49), and University College Hospital, London (8). It is believed that no similar review has hitherto been attempted in Britain. The commonest age at onset was 8 years, but 7 of the 62 patients (31 male and 31 female) were under one year when symptoms were first observed. One-fifth of the patients were Jewish.

The initial symptoms in order of frequency were rectal haemorrhage with diarrhoea (21 cases), diarrhoea alone (18), rectal haemorrhage alone (10), general ill-health (8), and pain in the abdomen (5). A history of salmonella or shigella infection was obtained in 3 cases, infective hepatitis in 4, and allergy in 3. Sibs of 2 patients had ulcerative colitis and there was a history of this condition in close relatives of 5 further patients. No definite psychological disturbances were noted. Sigmoidoscopy, which was performed in 56 cases, revealed abnormalities in 51; in the remaining 5 the distal colon and rectum appeared normal. Radiographs taken after a barium

enema in 47 cases showed that the whole colon was affected in 14 and the distal colon in 20; in the remaining 13 the appearances were normal. Initially the haemoglobin level was over 11.8 g. per 100 ml. in half the patients and less than 8.9 g. per 100 ml. in one quarter. The erythrocyte sedimentation rate was raised in more than two-thirds of the patients.

Systemic complications included arthritis (11 patients), clubbing (6), and hepatomegaly (4), while local complications included fissures and fistulae (8 patients), perforation (4), stricture (4), flexural hip deformity (2), and carcinoma (2 patients, aged 20 and 30 respectively). The authors point out that while the actual incidence of carcinoma in the series was 3.2% this must be regarded as a conservative estimate since the risk still remains in the younger patients.

Steroid therapy was given to 21 patients; of these 5 obtained a remission, 3 showed no improvement, and 2 died during treatment. The remaining 11 were still receiving steroids, 6 being well and symptom-free and 5 having a few symptoms. Operations, which were performed in 12 cases, included resection with anastomosis in 9, with excellent results, ileostomy (with resection) in one, ileostomy alone in one, and appendicostomy in one.

A review of the whole series showed that 5 children had died (4 could have been saved by surgery), one had severe symptoms, 19 had some symptoms, 31 were symptom-free, and 6 were well but still receiving steroids.

[This is an important paper.]

John Fry

366. The Effect of Furazolidone on the Intestinal Flora of Infants and Children

A. A. MINTZ. *Antibiotic Medicine and Clinical Therapy* [Antibiot. Med.] 7, 481-485, Aug., 1960. 4 refs.

A double-blind study with furazolidone in 65 children demonstrated both symptomatic and bacteriological effectiveness of this drug in the outpatient management of bacterial diarrhea, without significant alteration of the intestinal flora. Side effects were negligible and acceptability of the preparation was excellent.—[Author's summary.]

367. "Influenza Lung". (Die „Gripplunge“)

W. HARTMANN and F. SCHMID. *Zeitschrift für Kinderheilkunde* [Z. Kinderheilk.] 84, 235-243, 1960. 8 figs.

During the epidemic of "Asian" influenza-A of 1957-8 165 cases were admitted to the Paediatric Clinic of the University of Heidelberg. Of 114 uncomplicated cases 76 of the patients were newborn infants, 31 were aged 1 to 6 years, and 7 were school-children aged 7 to 14 years. Of the 51 patients with complications such as pneumonia or mixed infections (mostly staphylococcal), 46 were newborn, 4 were older infants, and one a child of school age.

From a radiological study of these cases the authors have given the name of "influenza lung" to a picture with the following consistent characteristics: (1) moderate enlargement of the hilum and especially of its upper pole; (2) increased linear markings in the upper pulmonary zones; (3) hyperillumination of the basilar and mid-zonal portions of the lungs; and (4) increased width

of the cardiac shadow towards both the right and the left. Certain variations of this picture were observed in the different age groups. In neonatal infants the upper border of the hilum may be blurred and there are increased linear markings around the upper pole of the hilum, and in some cases also around its lower pole on the right side. In older infants the radial markings are so increased that they give the appearance of a coarse network around the upper pole. Hyperillumination is most marked in the lateral aspects of the lower lung fields. In children of school age the hilum is not enlarged and the radial shadows are indistinct, but hyperillumination of the lower lung fields and enlargement of the cardiac shadow are well marked. Paradoxically, clinical evidence of cardiac dilatation in this age group was rarely present. When complications were present radiating hilar shadows were extensive and tended to coalesce to form large patches of varying density in the upper and midzones of the lung. This picture was met with almost only in the newborn and was more prominent in those with mixed infections than in those with pneumonia.

In the authors' opinion increased linear markings are indicative of inflammatory reaction in the reticular fibres of the lung, and since the influenza virus reaches them through the bloodstream they are more in evidence around the upper hilar pole and in the upper pulmonary zones. They are more prominent in very young infants, who have a more massive interstitial framework of reticular fibres in the lung than older children. Radiological evidence of "influenza lung" serves to confirm a diagnosis made on epidemiological and clinical grounds. It serves also to differentiate influenza (1) from other viral or bacterial infections of the nasopharynx, in which there is bilateral and symmetrical enlargement of the hilum due to enlarged bronchial lymph nodes, hyperaemia of the hilum, and exudation into the parahilar lung parenchyma; (2) from infections of the lower respiratory passages, in which radiating hilar shadows occur mainly round the lower pole of the hilum in the paracardial region, and are due to exudates into the lumen of the bronchi and inflammatory changes in the bronchial walls; (3) from other haematogenous and lymphatic infections, for example, atypical pneumonia, rubella, measles, bacterial pyaemia, and miliary tuberculosis, in which there is generalized enlargement of the hilum, especially of its upper pole, from involvement of the paratracheal and para-aortic lymph nodes. In none of these conditions is the increase of parahilar interstitial shadowing around the upper pole of the hilum so selective as in "influenza lung". In "measles lung", which is radiologically most similar to it, there is greater general involvement of the hilum and of the lung parenchyma.

E. S. Wyder

368. A New Method of Treatment of Tonsillitis in Children. (Новое в лечении ангины у детей)

N. I. NISEVIČ and V. S. KAZARIN. *Вопросы Охраны Материнства и Детства* [Vop. Ohrany Materin. Dets.] 5, 28-32, July-Aug., 1960.

Two new Soviet preparations, "anginol I" and "anginol II" have been tried in the treatment of 474 cases of tonsillitis, a group of 118 children with tonsillitis

which was treated with sulphonamides or antibiotics serving as a control. Anginol I consists of equal volumes of tinctures of aconite, peppermint, *Phytolacca decandra*, and *Echinacea purpurea*, and solutions of barium carbonate, calcium sulphate, and sulphathiazole 1:10, while Anginol II contains equal parts of tinctures of *Ailanthus*, belladonna, honeybee, *Mimosa pudica*, and *Echinacea purpurea*, and of solutions of mercuric cyanide (1 in 10⁻¹⁰) and sulphathiazole (1:10). The dosage was one drop per year of age up to the age of 5 plus one drop per each 2 years of age for children over 5, the maximum single dose being 10 drops. The two preparations were given alternately every 2 hours until abatement of pyrexia (2 or 3 days) and then 3 or 4 times a day for another one or 2 days.

This regimen resulted in a fall of temperature within 3 days in 94.4% of cases in the treated group compared with 75.2% in the controls. The local condition also cleared more rapidly and there was not a single case of local deterioration associated with general improvement, such as is sometimes observed in patients treated with sulphonamides or antibiotics. In 5.1% of cases the treatment was considered ineffective on the grounds that the pyrexia and pharyngeal signs persisted for 4 or 5 days. The corresponding proportion in the control group was 27.7%. Anginol thus proved more effective than antibiotics and sulphonamides in the treatment of lacunar and follicular tonsillitis, although it is noted that in phlegmonous and mycotic infections the results were poorer. No side-effects were observed.

It is stated that as a result of this and other clinical trials Anginol has now been approved by the Soviet Ministry of Health.

S. W. Waydensfeld

369. Bronchiolitis in Infancy

A. E. DUGDALE and M. McGEORGE. *New Zealand Medical Journal* [N. Z. med. J.] 59, 227-236, May [received Aug.], 1960. 3 figs., 38 refs.

Between 1946 and 1959, 17.3% of all children admitted to the Dunedin and Wakari Hospitals, New Zealand, had acute respiratory infections. Most of the children recovered satisfactorily, but in a small group with sudden and severe respiratory embarrassment there was rapid deterioration, death following within a few hours of admission. Initially these deaths were ascribed to bronchopneumonia, but reconsideration of the clinical and pathological features in these cases suggested that a more accurate diagnosis was bronchiolitis. Necropsy in 21 such cases showed that the lesions were principally in the bronchioles rather than in the alveoli. All except one of the infants were under 12 months old. The clinical course was similar in all cases: following an insignificant cold or snuffles in the prodromal phase there was sudden onset of alarming symptoms, consisting of laboured breathing, cyanosis, convulsions, and vomiting. The condition of the infants on admission, which was within 6 hours of the onset, was grave, with high fever up to 105° F. (40.6° C.) and tachypnoea of 60 to 100 respirations per minute; cyanosis was noted in 13 and an ashen grey pallor in 6. Examination of the chest revealed drawing-in of the lower intercostal spaces, but

often there were no adventitious sounds. Of the 21 infants, 19 died within 24 hours of admission.

As regards treatment of acute respiratory infections, in addition to the accepted measures, such as increased humidity of the atmosphere and administration of oxygen, fluids, and antibiotics, hydrocortisone was tried with good results, particularly in 8 severely ill patients who were given 100 mg. of hydrocortisone hemisuccinate intramuscularly every 4 hours.

The incidence of bronchiolitis in relation to bronchitis and bronchopneumonia was studied in the records of 72 infants under one year who were admitted consecutively for acute respiratory infection. Pneumonia was diagnosed in 17, bronchiolitis in 36, and bronchitis in 19. The authors conclude that the incidence of acute bronchiolitis is probably higher than has hitherto been thought and that in many cases in which "pneumonia" was diagnosed in the past the condition was bronchiolitis.

John Fry

370. Renal Vascular Hypertension in Children

J. P. SMITH and M. L. SAYLOR. *Journal of Urology* [J. Urol. (Baltimore)] 84, 17-23, July, 1960. 4 figs., 26 refs.

Renal vascular hypertension in children, with 4 illustrative cases, is discussed in this paper from Ohio State University College of Medicine and the Children's Hospital, Columbus, Ohio. It is pointed out that while essential or primary hypertension is rare in children and is treated medically, secondary hypertension is found more frequently and responds well to surgery. The renal disease which leads to secondary hypertension may be parenchymal, vascular, or perinephritic, but if the genitourinary tract is not at fault the trouble may arise in the central nervous, endocrine, or cardiovascular systems. The parenchymal disease producing hypertension in children may be glomerulonephritis, congenital malformation, embryonal carcinosarcoma (Wilms' tumour), or chronic pyelonephritis. Although there are no typical symptoms, the sudden onset of a persistently high blood pressure accompanied by albuminuria and leucocytosis suggests a renal vascular lesion. When only one kidney is affected the results of renal function tests are usually unchanged and excretory pyelography, followed, if necessary, by retrograde pyelography, is essential. If decreased renal plasma flow on the affected side suggests renal vascular obstruction, a unilateral decrease in urine flow and a reduction in sodium excretion will identify the affected side. A radioactive diiodine renogram is a painless procedure and may be of use in a young patient, while the suprarenal masses are outlined by the pre-sacral introduction of carbon dioxide in the retroperitoneum. Renal arteriography is valuable where vascular disease of the kidney is suspected, but needle biopsy is not suitable as a diagnostic procedure in cases of hypertensive kidney, although it has been employed in other renal diseases. Trans-abdominal open biopsy of both kidneys may be advisable to exclude bilateral disease. The cases described show that investigation of kidney function and surgery are indicated in children with renal hypertension, otherwise the kidneys will deteriorate.

J. Browne Kutschbach

371. Calcium Metabolism in Children with Hypothyroidism. (Untersuchungen zum Calciumstoffwechsel bei der Hypothyreose im Kindesalter)

K. LANG. *Monatsschrift für Kinderheilkunde [Mschr. Kinderheilk.]* 108, 395-398, Aug., 1960. 2 figs., 28 refs.

In this experimental study of the relationship between the thyroid gland and calcium metabolism in children the author, working at the Paediatric Clinic, University of Bonn, selected 6 children, aged from 2 months to 5 years, who were suffering from congenital hypothyroidism, had received no treatment with thyroid extract, vitamin D, or ultraviolet rays, and had had no recent infection, and in whom there was no increased calcium retention during convalescence which might confuse the results. Two days before starting the study a rigid diet of known calcium content was instituted and continued throughout. Before treatment with small doses of thyroid hormone, and also during it, the following data were obtained: (1) daily intake of calcium in the food; (2) daily excretion of calcium (in mg. per kg. body weight) in the stools (the urinary calcium excretion not being estimated as it was considered to be negligible); (3) daily amount of calcium retention in mg. per kg. body weight; and (4) the amount of calcium retention expressed as a percentage of the daily intake. During the study the daily intake of calcium varied from 50 to 124 mg. per kg. body weight.

When thyroid was administered the daily excretion of calcium in the stools was markedly raised in 4 cases, but not in the other 2, probably because the dosage was too low. In all cases before treatment the average daily calcium retention (which in healthy children of the same age is between 20 and 30 mg. per kg. body weight) was 56 mg. per kg., representing 57 to 75% of the daily calcium intake in the food. During hormone treatment these values fell to 35 mg. per kg. and 22 to 67% respectively. The author stresses that in untreated children with hypothyroidism calcium retention is high and dependent on the amount of calcium in the food. This factor must therefore be watched and the administration of medicinal calcium and vitamin D and the use of ultraviolet rays forbidden. In treated cases calcium retention is rapidly reduced, largely owing to increased excretion in the stools and the reduction is independent of dietary calcium intake.

E. S. Wyder

372. The Clinical Picture of the Sturge-Weber Syndrome in Children. (К клинике болезни Штурге-Вебера у детей)

R. B. ŠEJDIĆ. *Журнал Невропатологии и Психиатрии [Ž. Nevropat. Psihiat.]* 60, 836-840, No. 7, 1960. 3 figs., 4 refs.

The author describes 9 cases of the Sturge-Weber syndrome, recalling that the classic triad of signs in this condition consists of congenital angiomas of the face, congenital or early glaucoma, and angioma in one or other cerebral hemisphere. Areas of calcification in the brain may also occur, though generally not until after the third year of life, while other symptoms are convulsions, hemiparesis, and mental retardation. Of the 9 patients in this series, 6 had angiomas of the face

and scalp (in 4 cases also on the trunk and extremities), while all 9 suffered from hemiparesis, the angiomas being on the contralateral side. The paresis, however, had been present from birth in only one case; in 2 it followed a convulsion and in the other 6 it developed during the first or second year of life. Eight patients showed mental retardation. In one child, who died of Sonne dysentery, the angioma in the right cerebral hemisphere was found at necropsy. In only one case was any abnormality of the optic fundus present, and this was on the contralateral side. Calcification of the brain was demonstrated radiologically in 3 cases, again on the opposite side, that is, the side of the cerebral angioma.

Inquiry showed that in 4 cases there was a history of maternal trauma in the form of a fall or a blow upon the abdomen during pregnancy; another mother had undergone an operation under anaesthesia at the 5th month of gestation, while another had been poisoned by swallowing some "spirits" in the 2nd month. At birth 4 of the children had suffered from asphyxia, which may have an effect in precipitating the disease; but as the author remarks it is difficult to distinguish the condition from birth trauma or acute encephalitis in young children, especially as the cerebral calcification and eye changes do not develop until later. One child aged 12 had no convulsions, but she suffered from severe attacks of migraine.

L. Firman-Edwards

373. Studies in Febrile Seizures. V. Clinical and Electroencephalographic Study in Unselected Patients

J. G. MILLICHAP, J. A. MADSEN, and L. M. ALEDORT. *Neurology [Neurology (Minneapolis)]* 10, 643-653, July, 1960. 8 figs., 29 refs.

The purpose of this study was to determine the factors of importance in the aetiology and mechanism of febrile seizures on the basis of the clinical and electroencephalographic (EEG) findings in 110 unselected children examined at the Bronx Municipal Hospital Center, New York. Febrile seizures were approximately twice as common in boys as in girls, but no racial propensity was apparent. The first attack occurred most commonly between 6 months and 3 years of age. At the completion of the study attacks had recurred in 58 of the patients, but only 13 had had more than 4 attacks. The most frequent predisposing illnesses were acute throat infections (in 54%), otitis media (in 17%), and specific infections (in 13%). The mean temperature at the onset of the seizure was 104° F. (40° C.). The convulsions were of the tonic-clonic type in 85% and focal in 15%; they lasted less than 5 minutes in 43%, 5 to 10 minutes in 22%, 10 to 20 minutes in 19%, and longer than 20 minutes in 16%. Non-febrile convulsions were associated in 31 (29%) of the cases. Additional features were disordered behaviour in 35% of cases and recurrent abdominal pains in 21%, while allergic conditions were noted in 20%. There was a family history of fits in 30% of cases.

The EEG, which was obtained in 76 of the 110 cases, was normal in 52; in 18 seizure discharges were observed and in 6 "borderline" abnormalities.

John Fry

Public Health and Industrial Medicine

374. **The Content of Micro-elements in the Thyroid Glands of the Population and in the External Environment in the Endemic Goitre Region of Northern Bukovina.** (К вопросу о содержании микроэлементов в щитовидных железах и некоторых объектах среды обитания больных эндемическим зобом в Северной Буковине)

М. М. KOVALEV. *Проблемы Эндокринологии и Гормонотерапии* [Probl. Ėndokr. Gormonoter.] 6, 62-66, July-Aug., 1960. 10 refs.

Endemic goitre is prevalent in the mountainous districts of Northern Bukovina, and there is evidence that the presence of zinc predisposes to goitre in spite of an adequate intake of iodine. In this study several microelements of the soil and food products of the region were assayed spectroscopically and chemically, the metals investigated being manganese, cobalt, zinc, copper, and silver. The last two appear to have no effect on the incidence of goitre, while an inverse correlation was established between the content of manganese and cobalt and the incidence and intensity of goitre in the various areas. On the other hand it was demonstrated that there was a direct relationship between the incidence and degree of goitre and the content of zinc in the environmental materials assayed. Altogether 259 thyroid glands and 372 specimens of soil, drinking water, certain vegetables, and meat were examined for their content of the above elements, the study involving no fewer than 2,680 spectrographic analyses and 415 chemical assays.

Compared with conditions in the Carpathian mountains, the soil and food products of the eastern plains (where endemic goitre is rare) contain less zinc and more manganese, cobalt, and iodine. The content of zinc in the thyroid glands of goitrous inhabitants of the mountainous districts was lower than in those of normal subjects from the same area, but higher than that in the glands of inhabitants of the plain. The zinc content was higher in thyrotoxic than in euthyroid goitres in the same area, while that of manganese was lower in hyperthyroid cases than in euthyroid goitres and was lower in these than in healthy thyroid glands. The cobalt content on the other hand was lowest in normal thyroid glands, higher in euthyroid goitres, and highest in hyperthyroid cases. The highest content of copper was in the cases of cancer secondary to nodular endemic goitre. Parenchymatous goitres contained more of all five elements than those of the differentiated (colloid) type.

L. Firman-Edwards

375. **Poliomyelitis in the Vaccinated: England and Wales, 1958**

T. J. GEFFEN and C. C. SPICER. *Lancet* [Lancet] 2, 87-89, July 9, 1960. 10 refs.

All cases of poliomyelitis formally notified to the Ministry of Health in 1958 were analysed with particular reference to any previous history of vaccination against

poliomyelitis, the presence of paralysis, the site of paralysis in relation to the site of injection, and the interval between inoculation and the onset of disease. A total of 242 cases of poliomyelitis (137 paralytic and 105 non-paralytic) in vaccinated persons were reported. This represented about 12% of the corrected notifications, which numbered 1,994 (1,419 paralytic, 575 non-paralytic). Of the 242 patients, 64 had had only one dose of vaccine, 173 had had two doses, and 5 had had three. The disease developed within 28 days of the inoculation in 55 of the 64 who had received one dose and in only 25 of the 178 who had received two or more doses. Paralysis in the inoculated limb (left arm) was observed in 13 of the 54 in whom the paralysis occurred within 28 days of the last inoculation, but was part of a more widespread paralysis in 8; of the 83 in whom paralysis developed 28 days or more after the last inoculation, the inoculated limb was involved in 17, being the sole site of paralysis in 4 of them. Of the 129 deaths from acute poliomyelitis during the year, only 4 occurred in vaccinated subjects.

Analysis of the findings indicated that the vaccine did not cause "provocation" paralysis or "inoculation" poliomyelitis and that 2 or more doses of vaccine provided considerable protection, the disease developing in only 3.4 per 100,000 of the vaccinated compared with 21.1 per 100,000 unvaccinated persons.

A. Ackroyd

376. **Studies in the Epidemiology of Tinea Pedis. IV. Seed and Soil**

M. P. ENGLISH, M. D. GIBSON, and E. H. L. DUNCAN. *British Medical Journal* [Brit. med. J.] 2, 573-576, Aug. 20, 1960. 20 refs.

The infectivity of tinea pedis and the susceptibility of school-children to infection were studied in two separate groups attending senior schools in the Bristol area. The first group contained 67 boys known to have been infected with tinea pedis at the time of an earlier investigation (*Brit. med. J.*, 1959, 1, 1442; *Abstr. Wld Med.*, 1960, 27, 73). At the time of the present study 47 were cured, but 19 were still infected with *Trichophyton mentagrophytes* and one with *T. rubrum*. The next uninfected boy on the class register was taken as a control in each case. The second group contained 135 boys and 143 girls drawn from each of the four "school years" and chosen without consideration of their bathing habits or footwear. In this group 12 boys and 2 girls were infected with *T. mentagrophytes*. Footwear was then examined and bathing habits were investigated.

It was found that infected boys started to attend the local swimming baths at an earlier age than uninfected boys and that they used the baths more frequently. Most boys wore hot and heavy shoes and socks all the year round. No significant difference was observed between infected and uninfected boys in their use of showers, but showers were not taken regularly. In the

second group of boys and girls there was no significant difference in the age at which bathing started, but boys bathed more frequently out of school hours. The footwear of the girls was shown to be much lighter and cooler than that of the boys, especially in summer.

R. R. Willcox

377. Studies in the Epidemiology of Tinea Pedis. V. Some Day-schools Revisited

M. P. ENGLISH and M. D. GIBSON. *British Medical Journal* [Brit. med. J.] 2, 577-579, Aug. 20, 1960. 6 refs.

The authors have already described (*Brit. med. J.*, 1959, 1, 1442; *Abstr. Wld Med.*, 1960, 27, 73) the incidence of tinea pedis in children attending six senior day-schools in the Bristol area (five for boys and one for girls). In the present paper they report their findings when the schools were revisited. Of 1,456 boys examined, 5.5% were found to be infected compared with 7.1% in the earlier survey, and of 306 senior girls, 2% were infected compared with 2.2%. These differences were not considered to be statistically significant. *Trichophyton mentagrophytes* was responsible for 85.8% of the infections (83.5% in the first survey), *T. rubrum* for 4.7%, and *Epidermophyton floccosum* for 5.9%. Mixed infection was observed in 3 cases. In general, little change was noted in the incidence of lesions, infections, or fungus species in spite of the fact that the previous visits should have resulted in greater awareness of the condition by both staff and pupils.

At one boys' school in which adequate cleansing methods had been used in the swimming bath after the initial survey the incidence of tinea pedis fell from 8.9 to 4.5%, but at another the incidence remained at a high level. However, a much greater proportion of the boys at the first school had not visited the baths before the adoption of satisfactory cleaning measures, and at this school also athlete's foot had become a social stigma. Of 53 boys who were found to be infected at the time of the first visit, 45 were clear at the time of the second, indicating, apart from possible epidemiological considerations, that persistent infection is not a problem in individual boys.

R. R. Willcox

378. The "Cloud Baby": an Example of Bacterial-Viral Interaction

H. F. EICHENWALD, O. KOTSEVALOV, and L. A. FASSO. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] 100, 161-173, Aug., 1960. 9 figs., 14 refs.

A new concept of the epidemiology of bacterial disease is presented in this paper from the New York Hospital-Cornell Medical Center. A study of quantitative data on airborne dissemination of *Staphylococcus aureus*, in which air-sampling methods with high-velocity liquid impingers and sieve samplers were used, suggests that some infants contaminate the atmosphere and are surrounded by "clouds" of bacteria. In the experiments described herein it was found that infants could be divided into three groups: (1) the majority, from whom no bacteria could be isolated; (2) a large group who were asymptomatic, but nasal and skin carriers of Type-80/81 *Staph. aureus*; and (3) a small group who, in addition

to being carriers, had obvious pyoderma. Further study of Group 2 showed that a proportion of these infants disseminated staphylococci and that the air surrounding them contained clouds of organisms. It was further shown that the skin and umbilical cord played no significant part in contaminating the air and that spread occurred through the respiratory tract. Epidemiological experiments illustrating the part played by these "cloud babies" in the aetiology of epidemics of staphylococcal infection in nurseries are described.

It was also shown that a "cloud factor" exists independently of the staphylococcus and that this cloud factor is probably a virus. In one epidemic adenovirus Type 2 was isolated from some infants and in another ECHO virus Type 20 was recovered. It is postulated that the phenomenon represents an unusual but highly important interaction between viruses and bacteria and that the viruses facilitate the spread of bacteria.

[This paper is an important one and must be read in its entirety.]

John Fry

379. Chronic Alcoholism among Parisian Workers.

(L'alcoolisme chronique chez les travailleurs parisiens) V. RAYMOND and C. BARUCH. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [Arch. Mal. prof.] 21, 413-427, July-Aug., 1960.

In this investigation of the incidence of alcoholism among 552 workers (403 male and 149 female) aged between 16 and 50 in one district of Paris the diagnosis of alcoholism was based only on physical examination and on information obtained from the workers themselves as to their actual consumption of alcohol, the latter details being of course impossible to verify. The significant physical signs were considered to be the presence of an enlarged liver and of tremor.

It was found that 110 men and 6 women could be classed as alcoholics, the incidence being thus much higher among the males (27%) than among the females (4%). The male subjects included one youth aged 16 and 13 men aged between 18 and 30 years. These 14 men and the 6 women are described in detail. Inquiry showed that previous disturbances of health included gastrointestinal disorders (dysentery, colitis, and peptic ulcer) in 46%, surgical operations (appendicectomy, herniotomy, cholecystectomy, or gynaecological procedures) in 27%, pulmonary disorders (tuberculosis, chronic bronchitis, sclerosis, or emphysema) in 6%, accidents (including fractures) in 8%, and cardiovascular disorders (especially hypertension) in 2%.

An assessment of the relation between occupation and chronic alcoholism showed that the greatest amount of wine was consumed by lorry drivers, followed by shop assistants and then salesmen; office workers consumed least of all, while of the workers on special industrial processes, spray painters had the heaviest consumption. The influence of diet was indicated by the fact that the alcoholics had an inadequate or no morning meal; they ate less meat and more bread and had a preference for thirst-provoking articles of diet such as sauces, ragouts, and spices, and they drank more wine between meals, more beer during work, and smoked more cigarettes.

Heavy muscular work was clearly related to alcoholism, more than two-thirds of the alcoholics being so employed. Prolonged hours of work and difficulties of transport to and from work in bad weather also led to a higher consumption of wine in the winter and of beer in the summer.

The actual consumption admitted by the 20 individuals whose cases are described in detail was generally between one and 2 litres of red or white wine daily with meals, but often with the addition of 2 or 3 extra glasses of wine, aperitifs, and a litre of beer or cider. Most of the workers considered this amount to be normal and even to be essential. The quantity consumed could not in all cases be correlated with the clinical findings of enlarged liver and tremor. It is noted that the erroneous idea that the quantity admittedly consumed was harmless and indeed was indispensable for health and well-being led in some cases to an expenditure of one-quarter to one-third of the worker's monthly salary on alcoholic beverages.

Ethel Browning

INDUSTRIAL MEDICINE

380. **The Risk of Mercurial Poisoning in the Manufacture of Thermometers.** (Les risques d'hydrargyrisme dans les ateliers de fabrication de thermomètres) G. JENNY, A. J. CHAUMONT, E. WEIL, and G. JENNY. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [Arch. Mal. prof.] 21, 439-455, July-Aug., 1960. 5 figs., 42 refs.

As metallic mercury is practically non-toxic the essential point in the toxicology of mercury is its property of emitting vapour even at ordinary temperatures. The severity of mercury poisoning depends essentially on the time of exposure to, and the concentration of, mercury vapour in the atmosphere. The present universally accepted maximum concentration is 0.1 mg. per c. metre of air for 7 to 8 working hours. This paper reports an investigation at the Institute of Legal and Social Medicine, Strasbourg, into the conditions in four factories making thermometers. An examination of 36 workers, involving estimations of their urinary excretion of mercury, suggested that the accepted safety limit should be fixed at a lower level. The authors remark that almost the only improvement in working conditions in thermometer manufacture during the present century has been the introduction of automatic filling in the cold and in closed vessels. Even those workers not directly engaged in manipulation of the metal, but employed in glass blowing and in calibration, closing, engraving, and finishing of the thermometers, are exposed to risk. This was so in 3 of the 4 factories, which were small "artisan" establishments where the mercury was kept in containers not hermetically sealed, the tables and floor were contaminated with droplets of mercury, the walls and ceilings of the small unventilated rooms were covered with dust, and purification of recovered mercury was carried out by hand without any protective measures. In the one larger establishment the conditions were much more favourable, separate rooms being used for the non-

hazardous operations and all rooms being clean and provided with down-draught exhaust ventilation at the work-tables. Nevertheless the incidence of mercurialism in this well-run factory was 22.6%, ranging up to 55.5% in the three small factories.

The predominant symptom of intoxication is mercurial sensitivity, which was present in 15 (41%) of the 36 workers examined, producing asthenia, anorexia, loss of weight, a tendency to syncope, and frequent headaches. Tremor, present in 13 (36%), was associated with the characteristic illegible handwriting (illustrated). Other symptoms included exaggerated reflexes, neuralgia, neurovegetative disorders, albuminuria, ocular disturbance, pyorrhoea alveolaris, loss of teeth, neuroses, and hyperthyroidism. There appeared to be no relation between intoxication and sex, age, or duration of exposure. Investigation of mercury excretion in the urine was carried out qualitatively by a modification of Reinsch's test and quantitatively by a method based on the reduction of metallic mercury by hydrazine and copper sulphate. Spectrographic examination was made by either the diphenyl carbazide or the dithizone method, the latter, with an acid medium, being preferred as it avoids the loss of mercury in the precipitate of urinary phosphates and urates caused by an alkaline medium. The results were interpreted as showing a definite relation between the urinary mercury level and the clinical symptoms of mercurialism. Two young subjects, who had worked in the factory for about a year without developing any symptoms, but who had high urinary excretion levels of mercury and were considered to be examples of mercurial hypersensitivity, were recommended to change their occupation.

The authors consider that since minute quantities of mercury are probably present in the urine of most human beings, amounts below 20 µg. per litre are not pathological, but that above this level careful examination for slight symptoms should be made; if the level is above 30 µg. per litre intoxication is probably present. They conclude with a number of practical suggestions for the improvement of working conditions in factories where mercury is used.

Ethel Browning

381. **Dermatitis of the Hands in Ladies' Hairdressers** J. JAMES and C. D. CALNAN. *Transactions of the St. John's Hospital Dermatological Society* [Trans. St. John's Hosp. derm. Soc. (Lond.)] No. 42, 19-42, 1959. 8 figs., 35 refs.

The problem of occupational dermatitis in ladies' hairdressers was investigated at St. John's Hospital for Diseases of the Skin, London, with particular reference to the materials used in hairdressing and the findings in 100 employees (32 male and 68 female) who developed eczema of the hands. More than half of the patients were under 35 years of age and one-third had a personal or family history of atopy. From the results of patch tests and a study of the history and pattern of the dermatitis the condition was classified as follows: allergic contact sensitivity, 23 patients; primary irritant dermatitis, 61; and a constitutional eczema in addition to an irritant dermatitis, 16. The materials used included

shampoos, rinses, conditioners, permanent-waving preparations, dyes, bleaches, setting preparations, lacquers, tonics, and lotions. In the early stages recognizable features were to be seen in relation to the cause as a result of the different ways the materials were handled, typical patterns being associated with shampoos, thioglycollate, and rubber gloves.

In the authors' view there are four factors which would assist in reducing the incidence of this variety of dermatitis: (1) more careful selection of those taking up hairdressing, with recognition of the fact that individuals with a past or family history of eczema or asthma are likely to have trouble with their hands "on doing wet work"; (2) raising the standard of training—the efficiency of the "trained" hairdresser was found to vary considerably; (3) better instruction in the care of the hands, including careful rinsing and drying after each procedure and regular use of barrier creams and rubber gloves for permanent waving and dyeing; and (4) more careful use of materials, with strict adherence to the manufacturer's instructions, especially certain cold-wave lotions and hydrogen peroxide.

The authors' findings suggest that shampoos and thioglycollate preparations are the principal causes of primary irritant dermatitis and that the important sensitizers are "para-" dyes and rubber gloves; the role of thioglycollate as a sensitizer is uncertain. In a follow-up study of 77 of the patients it was found that 14 had given up hairdressing because of dermatitis. *R. G. Meyer*

382. Decontamination of Human Skin Experimentally Soiled by Radioactive Materials

J. S. FELTON and C. J. ROZAS. *Archives of Environmental Health* [Arch. environm. Hlth] 1, 87-95, Aug., 1960. 2 figs., 6 refs.

The development of an effective cleansing material for the removal of radioactive contaminants from the skin has presented many difficulties. In the study here reported from the School of Public Health (University of California), Los Angeles, various cleansers used for the removal of common industrial skin contaminants were tested, the radioactive isotopes of iodine (^{131}I) and phosphorus (^{32}P), diluted with 95% ethyl alcohol to a concentration of 1 $\mu\text{c.}$ per ml., being employed as contaminating agents. To ensure uniformity in the tests a mechanical scrubbing device fitted with a felt pad and having an action regulated to deliver 100 strokes per minute was used to apply the cleanser over an area measuring 3 \times 3 cm. on the skin of the palm and the forearm (the most frequently contaminated sites) which was demarcated by laundry ink. The radioactive solution, 0.05 $\mu\text{c.}$ at a time, was applied with a calibrated medicine dropper and evenly distributed by means of a glass rod. The background radiation and the level of base-line radioactivity were determined by a Geiger-Müller counter. After application of a predetermined quantity of cleanser each site was given 3 one-minute scrubbing, the residual activity being measured after each scrub. The substances tested included two types of commercial cleanser, seven granular and four waterless, a water slurry of titanium dioxide, and a homo-

genous cream containing a powdered detergent, versene, carboxymethyl cellulose, and water. The effect of the previous application of protective materials such as silicone or lanoline lotion was also tested, but neither of these proved significantly effective in limiting the absorption of the contaminant.

It was found that contamination with ^{131}I was the more difficult to remove, though the removal of both isotopes was effected by the granulated cleansers with a high degree of efficiency (99.6% for ^{32}P and 99% for ^{131}I). An additional final washing with a granular cleanser returned the level of radioactivity to the initial background count. None of the cleansers caused any residual skin lesions. The granular type of commercial skin cleanser was superior to the waterless type and is recommended for use in laboratory and industrial operations in which radioactive contamination of the skin may occur. *Ethel Browning*

383. Occupational Disease in California Attributed to Pesticides and Agricultural Chemicals

G. D. KLEINMAN, I. WEST, and M. S. AUGUSTINE. *Archives of Environmental Health* [Arch. environm. Hlth] 1, 118-124, Aug., 1960. 4 refs.

Occupational disease occurring in persons handling chemical substances is widespread. It has been estimated that about one-fifth of the total quantity of pesticides manufactured in the U.S.A. are used in California. Numerous accounts of occupational disease caused by these compounds and by related substances employed in the agricultural industry have appeared in the literature.

Among the most hazardous chemicals are the organic phosphates, particularly nitrophenylthiophosphate ("parathion"), tetraethylpyrophosphate (TEPP), ethyl mercapto- and ethyl diethyl-thiophosphate ("demeton", "systex"), and carbomethoxymethylvinyl dimethyl phosphate ("phosdrin"). This paper reviews the report issued by the State Department of Public Health, California, which states that in 1957 nearly one-third of the 749 cases of occupational disease attributed to agricultural chemicals were caused by organic phosphates. Halogenated hydrocarbons (dicophane (DDT), endrin, aldrin, methyl bromide, and carbon tetrachloride) accounted for 10% of the cases, weed killers (exclusive of cyanamide) for 9%, fertilizers for 5%, and unspecified substances for 18%.

Dermatitis (excluding burns) was recorded in 55% of the physicians' reports, systemic poisoning in 34%, respiratory illness in 8%, and other unspecified diagnoses in 4%. Of the 412 cases of occupational dermatitis, over 40% were ascribed to unspecified chemicals, 15% to weed killers, including cyanamides, 10% to the halogenated hydrocarbon pest killers, and 8% to both organic phosphate pest killers and to fertilizers.

There was one fatality attributed to demeton after the cleaning of an airplane used for crop dusting. The patient died within 5 hours of reporting illness to his employer. The diagnosis of organic phosphate poisoning was confirmed by the low levels of plasma and blood cholinesterase found. *Ethel Browning*

Forensic Medicine and Toxicology

384. **The Importance of Subendocardial Extravasations.** (Sur les suffusions sous-endocardiques et leur importance) O. JELACIC and V. KANJUH. *Annales de médecine légale et de criminologie, police scientifique et toxicologie* [Ann. Méd. lég.] 40, 316-334, July-Aug., 1960. 1 fig., 16 refs.

The authors, working at the University and Army Institutes of Pathology and Legal Medicine, Belgrade, have performed [over an unstated period] 3,178 necropsies for both routine and medico-legal purposes, that is, in cases of both natural and violent death; 2,328 were on males and 850 on females. Out of this total, subendocardial extravasations (S.E.) were found in 270 males and 54 females. Some of these were situated under the endocardium of the left ventricle on the inter-ventricular septum and some on the anterior and posterior walls. A remarkable fact is that although many authors have reported the finding of such extravasations in newborn infants, none was found in any of the 222 neonates examined in this series.

These extravasations are regarded as vital phenomena, as was shown by a leucocytic reaction around the lesions, evidence of former haemorrhage, and signs of commencing regeneration, although they may also appear immediately after trauma, being present in 65 out of 164 cases of instantaneous death. An important point was the agreement between the clinical and electrocardiographic signs of disturbances of cardiac conduction and the histological evidence. The extravasations were observed most frequently in association with conditions in which haemorrhages of various kinds or a sudden fall in arterial pressure due to a cardiovascular lesion had occurred and in cases of cranial injury. They were also found in 3 out of 5 patients dying from eclampsia and in 2 out of 5 dying from diphtheria. No case was seen in which the rise in intracranial pressure had been gradual.

In regard to the pathogenesis, irritation of the vagus may well be the prime cause, but exaggerated myocardial contractions are considered to be mainly responsible, though their production is aided by the physiological stasis in the subendocardial vascular plexus during systole and the laxity of the connective tissue surrounding the left branch of the bundle of His. In none of the present cases were these extravasations the actual cause of death. Asphyxia is not so important as has been supposed, none being found in 74 drowned persons. It is concluded that they have a relative diagnostic value, being characteristic, but not pathognomonic, of cases in which extravasation of blood or a rapid rise in intracranial pressure has occurred. W. K. Dunscombe

385. Drug-induced Jaundice

A. G. MELROSE. *Scottish Medical Journal* [Scot. med. J.] 5, 250-256, June, 1960. 3 figs., 47 refs.

The common forms of iatrogenic jaundice are described in this paper from the Southern General Hospital, Glasgow. The author states that since the aetiology of

drug-induced jaundice is unknown the classification of the different types should be based upon the observed pathological lesions characteristic of each rather than upon theoretical concepts. The classification suggested and discussed is: (1) cholangiolitic, (2) cholestatic, and (3) hepatic.

Cholangiolitic jaundice may be produced by arsenic, chlorpromazine (by far the commonest agent) and other phenothiazine derivatives, chlorpropamide, thiouracil, and *para*-aminosalicylic acid. Prodromal symptoms include fever, upper abdominal pain, and pruritus, together with an eosinophilia. Jaundice follows and lasts, on the average, 4 to 6 weeks; some cases prove fatal. Biochemical tests indicate the presence of biliary obstruction without hepatic cell damage. On histological examination the parenchymal cells are found to be normal, but the bile ductules contain bile casts and there is round-cell infiltration of the portal tracts.

Cholestatic jaundice has been observed following administration of methyltestosterone, norethandrolone, or carbimazole. The icterus lasts many weeks, but there is usually recovery in these cases. Histologically, the only difference from cholangiolitic jaundice is the absence of portal-tract inflammation. The nature of the lesion may be due to interference with a biochemical transport mechanism by a metabolite of the drug given, and the author considers that hypersensitivity to the drug may be the cause.

Hepatic jaundice from such drugs as the sulphonamides, phenytoin sodium, troxidone, and iproniazid is not uncommon. Jaundice due to iproniazid sometimes proves fatal (according to different authors the mortality is 15 to 30%) and is clinically and morphologically indistinguishable from viral hepatitis. Prednisolone often hastens recovery in hepatic jaundice.

W. H. Horner Andrews

386. Peritoneal Dialysis in Salicylate Intoxication

G. B. ELLIOTT and J. U. CRICHTON. *Lancet* [Lancet] 2, 840-842, Oct. 15, 1960. 10 refs.

Writing from the General Hospital, Calgary, Canada, the authors describe 3 cases of severe salicylate intoxication successfully treated by peritoneal dialysis. Of the 3 patients, 2 were children aged 5 months and 30 months respectively and one was an adult of 21 years. The fluid used for dialysis was Hartmann's solution (130 mEq. sodium, 40 mEq. potassium, 2.7 mEq. calcium, 109 mEq. chlorine, and 28 mEq. lactate per litre). Dextrose was added to the dialysing solution as required to prevent depletion.

With this procedure salicylate was removed directly. All the patients showed serious potassium depletion which was corrected by dialysis. Peritoneal dialysis is advocated by the authors as an alternative to the artificial kidney in such cases, where speed and simplicity are essential. H. B. Stoner

Anaesthetics

387. Intravenous Lidocaine as an Adjunct to General Anaesthesia: a Clinical Evaluation

O. C. PHILLIPS, W. B. LYONS, L. C. HARRIS, A. T. NELSON, T. D. GRAFF, and T. M. FRAZIER. *Anesthesia and Analgesia; Current Researches* [Anesth. Analg. curr. Res.] 39, 317-322, July-Aug., 1960. 12 refs.

The value of lignocaine as an adjuvant to general anaesthesia was studied at the Hospital for Women, Baltimore, in 2 groups of patients—those undergoing minor perineal operations and those subjected to major operations in the pelvic region. In the former group premedication was with 5 mg. of perphenazine and 0.4 mg. atropine; anaesthesia was induced with not more than 200 mg. of thiopentone followed by nitrous oxide and oxygen, this being supplemented by lignocaine (250 mg. by intravenous infusion) in about half the patients, while the remainder received a solution of a placebo. In both groups additional thiopentone was administered if necessary to maintain smooth anaesthesia. For the patients undergoing major pelvic operations premedication was with morphine, atropine, and perphenazine; anaesthesia was induced with thiopentone, a total of 500 mg. being generally given. Nitrous oxide and oxygen were then administered in semi-open circuit. About half the patients were also given a continuous infusion of 0.05% suxamethonium and 0.1% lignocaine (average total dose of the latter being 734 mg.), while the remainder received an infusion of a placebo. It was found that the patients undergoing minor operations who received lignocaine required an average of 387 mg. of thiopentone as against 439 mg. of thiopentone in the placebo group. Smooth anaesthesia was achieved in a higher proportion of cases in the lignocaine group; there was no difference in the recovery time. Patients subjected to major operations who received lignocaine required significantly less suxamethonium than those who had received a placebo. The recovery times and postoperative analgesic requirements were, however, similar in both groups.

Mark Swerdlow

388. The Solubility of Volatile Anaesthetics in Oil

J. F. NUNN. *British Journal of Anaesthesia* [Brit. J. Anaesth.] 32, 346-352, Aug., 1960. 8 figs., 8 refs.

Practical studies show that the solubility of chloroform in oil deviates markedly from the behaviour expected according to Henry's law. An equation has been derived from Raoult's law from which it is possible to predict the solubility of chloroform in a given oil. Over the clinical range the predicted results agree well with those derived experimentally. The equation enables the equilibrium uptake of anaesthetic by the body fat to be determined theoretically and quantifies the action of the depot fat as a capacitance. At a first approximation, the apparent solubility of an anaesthetic in fat is related to the reciprocal of its vapour pressure. Thus the obser-

vations of Meyer and Hemmi (1935) are in accord with the expression of potency in terms of chemical potential (Ferguson, 1939).

The equation may be used to derive the oil-water solubility coefficient of anaesthetic agents and the predicted values are in accord with those determined experimentally.—[Author's summary.]

389. A Local-anaesthetic Solution with Longer Action

R. E. LODER. *Lancet* [Lancet] 2, 346-347, Aug. 13, 1960. 1 ref.

As a result of several experiments designed to produce local as distinct from general analgesia after operation the author found that a 1% solution of lignocaine in 10% "dextraven" (10% dextran and 5% glucose in water) with 1:250,000 adrenaline gave analgesia lasting 10 hours. For a trial of this solution patients subjected to thoracic and abdominal operations and haemorrhoidectomy were chosen because the wounds are especially painful. At the end of the operation the solution was injected subcutaneously around the edge of the wound or into the sensory nerves supplying the part. The patient was given an analgesic after returning to the ward if this was thought necessary, the interval elapsing before administration of the analgesic being used to gauge the success of the treatment.

No general or local reaction and no wound sepsis occurred. The patients subjected to intrathoracic operations and to haemorrhoidectomy were much improved with local analgesia postoperatively because they were free from pain, and those with thoracic incisions were able to inspire deeply. The results in patients with abdominal wounds depended on the severity of the operation performed; patients subjected to operations on the common bile-duct and gall-bladder and those operated on for peptic ulceration "had an ill-defined uneasy feeling inside the abdomen".

M. Woods

390. Anaesthesia and Recovery in Patients Undergoing Commissurotomy for Mitral Stenosis. (Anesthésie et réanimation dans la commissurotomie pour rétrécissement mitral)

P. FERTIL, F. NICOLAS, and E. CORNET. *Poumon et le cœur* [Poumon] 16, 549-558, June-July [received Oct.], 1960. 3 figs., 5 refs.

The authors describe the anaesthetic technique employed in 100 patients, 86 female and 14 male, aged from 14 to 58 years, undergoing mitral valvotomy. The problems inseparable from thoracic surgery in general, namely, the open chest, disturbance of ventilation, and reflex stimulation, are briefly discussed. The anaesthetic technique consisted in premedication with sparteine, morphine, and scopolamine followed by induction with thiopentone and a relaxant (D-tubocurarine in 97 cases, gallamine being used in 3 only because of its

effect on the heart rate). Intubation was performed with an analgesic lubricant, but no analgesic spray was employed. Maintenance was with nitrous oxide and oxygen plus intermittent thiopentone and the relaxant. Only a moderate fall in blood pressure occurred when the thiopentone was well diluted and given slowly and the patient well oxygenated. No vasopressor drugs were necessary. The dosage of tubocurarine varied from 6 to 35 mg., that of thiopentone from 0.5 to 1.2 g. The concentration of nitrous oxide (50% with oxygen) was increased during closure of the chest to obviate the need for more thiopentone.

Cyanosis of the extremities was noted in many cases, but usually improved on completion of the valvotomy. The systolic blood pressure (90 to 100 mm. Hg on arrival at the theatre) often fell after intubation, incision of the pleura, opening the pericardium, valvotomy, and approximation of the ribs, and sometimes rose during periods of hypoventilation: if the systolic pressure did not fall below 70 mm. Hg no treatment was considered necessary. Haemorrhage necessitated whole-blood transfusion, but overtransfusion was carefully avoided. In 8 cases a transitory rise in blood pressure followed digital exploration of the valve. Arrhythmias were seldom seen except during handling of the heart, when ventricular ectopic beats, sinus tachycardia, nodal rhythm, nodal ectopic beats, rarely flutter or fibrillation, and exceptionally a complete atrio-ventricular block might occur. The treatment of these disturbances of rhythm and the electrocardiographic findings are described.

Extubation was usually possible at the end of the operation, and early recovery of consciousness was the rule. There was delayed return of consciousness in 4 patients, of whom 2 developed a left hemiplegia (fatal in one case), one regained consciousness, but soon relapsed into coma and died 12 hours later of massive pulmonary embolism, and one developed severe cyanosis which proved to be due to a left pneumothorax. No other patients died. A postoperative fever (up to 40° C. (104° F.) in a few cases) during the first 5 days was common, but persistence of the fever beyond this time indicated excessive pleural fluid requiring paracentesis (7 cases), altered coagulability of the blood (6 cases), or pulmonary embolism (2 cases); there was no case of overt phlebitis and no infection. Postoperative hypotension was usually due to bleeding, but overtransfusion was continually guarded against. Postoperative atrial fibrillation occurred in 12 cases and sinus tachycardia in 17, and required digitalization.

[These results are remarkably good, but no mention is made of the selection of cases or of the preoperative digitalization of patients in atrial fibrillation.]

D. D. C. Howat

391. Experiences with Cardiac Catheterization Using Halothane-Compressed-air Anesthesia

M. L. NORTON and Y. KUBOTA. *Anesthesiology* [*Anesthesiology*] 21, 374-379, July-Aug., 1960. 14 refs.

Anaesthetic agents for cardiac catheterization must be non-explosive and have high potency and a smooth, steady action; they should not interfere with blood gas

analyses, and recovery should be rapid and smooth. In anaesthesia for this purpose the blood oxygen concentration should be constant and the airway controlled, and narcotics which disturb cardio-respiratory physiology should be avoided. At the University Hospital, New York, 38 patients were anaesthetized 54 times; induction and maintenance of anaesthesia were accomplished by inhalation techniques only, halothane being vaporized by compressed air. It was found that the exposure of the anaesthetist's hand to radiation was within safe limits. The agent did not interfere with blood gas analyses, as shown by readings taken in the conscious and in the anaesthetized patient. Electroencephalographic levels 1 to 3 were found to be an accurate and useful guide in the darkened room.

Since this series the authors have used halothane and 100% oxygen during cinecardiography and angiocardiology to lessen tissue hypoxia in case of a block in the cardiovascular system.

W. Stanley Sykes

392. The Concentration of Anaesthetics in Closed Circuits, with Special Reference to Halothane. I. Theoretical Study

W. W. MAPLESON. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] 32, 298-309, July [received Sept.], 1960. 9 figs., 16 refs.

The factors influencing the concentration of an anaesthetic agent inspired by the patient from a closed-circuit machine are described in the first of these three papers from the Welsh National School of Medicine, Cardiff. The author states that complete equilibrium is attained only when the body is saturated with the agent at the inspired tension. After a relatively high initial uptake the rate of uptake thereafter falls fairly rapidly at first and then more and more slowly, but reaches zero only after many hours. Factors influencing the concentration of the anaesthetic in the circuit are the presence of leaks in the apparatus, the volume of input of fresh gases, the position of the inspiratory valve in the circuit, the minute volume ventilation, the patient's oxygen consumption, and the nature of the vaporizer. An important point is the position of the vaporizer in relation to the circuit; it may be outside (V.O.C.) or at one of at least three positions within the circuit (V.I.C.).

An appendix to the paper deals with the performance of these circuits and shows how the inspired and alveolar concentrations vary with the different factors involved.

J. D. Laycock

393. The Concentration of Anaesthetics in Closed Circuits with Special Reference to Halothane. II. Laboratory and Theatre Investigations

S. GALLOON. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] 32, 310-323, July [received Sept.], 1960. 18 figs., 6 refs.

This second paper from Cardiff [see Abstract 392] describes experiments carried out with halothane in the laboratory and observations in the operating theatre to confirm the theoretical conclusions presented in the first paper. An adjustable pump in place of the patient's

respiration and three different absorption circuits were used under conditions simulating those met in practice, the concentrations of halothane being measured by means of a galvanometer technique. Some discrepancies arose from absorption of halothane by the rubber in the circuit, which took some hours to become saturated. Experiments with the vaporizer inside the circuit are first described, the four variables investigated being the time from the start of the experiment, the tap setting on the vaporizer, the fresh-gas flow, and the minute volume ventilation. A number of graphs are presented to demonstrate the effect of these factors on halothane concentrations with various types of absorbers.

(1) A rapid rise was demonstrated in the inspired concentration for the first 10 minutes and an almost steady level was attained after 20 minutes. (2) An increase in the tap setting of the vaporizer produced a marked increase in concentration with only a small movement of the tap. (3) Increase of fresh-gas flow, especially above basal levels, caused a fall in concentration which was due to escape through the expiratory valve. (4) The concentration of inspired anaesthetic varied with the minute volume ventilation and was much increased by manual inflation. The experiments were repeated with the vaporizer outside the circuit, using Waters's to-and-fro system. The principal difference was that in the laboratory increased ventilation did not increase "inspired" concentration of the anaesthetic, whereas in the theatre this concentration was decreased, although the alveolar concentration and hence the depth of anaesthesia were both increased.

J. D. Laycock

394. The Concentration of Anaesthetics in Closed Circuits with Special Reference to Halothane. III. Clinical Aspects

W. W. MUSHIN and S. GALLOON. *British Journal of Anaesthesia* [Brit. J. Anaesth.] 32, 324-333, July [received Sept.], 1960. 8 figs., 9 refs.

In this paper the theoretical and experimental considerations described in the two preceding papers [see Abstracts 392 and 393] are applied to the clinical use of halothane in closed-circuit anaesthesia. It is pointed out that in order to effect economy in the amount of halothane used a small gas flow must be employed. This is an argument for using oxygen without nitrous oxide, as extreme economy of halothane is incompatible with fine control of the inspired concentration.

Criteria for including a vaporizer in the circuit are laid down. The concentration produced by it should be known and constant for each tap-setting, and should be independent of variations in the amount of gas flowing through it. Efficiency should be low for the vaporizer inside the circuit (V.I.C.)—up to 2% is adequate. It should be up to at least 6% when the vaporizer is outside the circuit (V.O.C.) so that small nasal flows are practicable. The tap should allow of fine control, and the air space above the liquid should be small to avoid the sudden inhalation of a high concentration of gas when the vaporizer is turned on. The nearest approach to these ideal standards is best achieved with a machine which has been designed expressly for halothane. Those

designed for ether give a less fine adjustment of concentration. With the vaporizer in the circuit (V.I.C.) ventilation is one of the most important factors influencing the inspired concentration. In spontaneous respiration the sequence of light anaesthesia with deep respiration leading to increased concentration and deeper anaesthesia is a valuable, and to some extent an automatic, safety factor. With controlled respiration, however, this principle no longer holds and it is essential to adjust the tap or increase the gas flow to avoid overdosage. Failure to do this may have been a factor in some reported fatal cases. With the vaporizer outside the circuit (V.O.C.) changes in ventilation have little effect on the depth of anaesthesia with flows of 4 litres per minute or more.

Estimation of the inspired concentration is obviously helpful in achieving a proper use of halothane in a closed circuit, but it is complex because of the various factors discussed, especially with V.I.C. With V.O.C. the inspired concentration is always less than that in the vaporizer. A "build-up" in the concentration within the circuit is naturally to be feared, but since equilibrium is established within 20 minutes signs of overdosage will be seen within this time. It is emphasized that the use of halothane in a closed circuit is safe only if the factors discussed are borne in mind. The less experienced anaesthetist is advised to use a calibrated and thermostatically controlled vaporizer outside the circuit, especially if controlled respiration is contemplated.

J. D. Laycock

395. Effect of Epinephrine upon the Duration of Spinal Anaesthesia

L. D. EGBERT and T. C. DEAS. *Anesthesiology* [Anesthesiology] 21, 345-347, July-Aug., 1960. 8 refs.

Adrenaline prolongs local anaesthesia by local vasoconstriction. Since it has been suggested that adrenaline is a possible cause of ischaemic tissue damage an attempt was made to find the optimum dose of this drug for spinal anaesthesia, 0.1, 0.2, 0.3, 0.4, or 0.5 mg. being added to standardized doses of tetracaine and dextrose. In 137 patients the duration of anaesthesia, as measured by a fall of two dermatomes, was prolonged increasingly up to the maximum dose used. It was not possible to predict the duration accurately in individual patients.

W. Stanley Sykes

396. Anileridine in Anaesthesia: a Clinical Trial

M. SWERDLOW, P. R. BROWN, and A. TETLOW. *Anaesthesia* [Anaesthesia] 15, 280-288, July, 1960. 1 fig., 10 refs.

Anileridine and pethidine were each used in 120 patients (aged 18 to 60) to supplement thiopentone-nitrous oxide-oxygen anaesthesia. A standard dose of thiopentone (7 mg. per kg. body weight) was administered, and no muscle relaxants were given in the maintenance of anaesthesia. After induction of anaesthesia with thiopentone, nitrous oxide (6 litres per minute) and oxygen (2 litres per minute) were administered in semi-open circuit. An initial dose of analgesic was injected and thereafter supplementary doses of analgesic were given as indicated by signs of lightening anaesthesia.

It was found that anileridine was as effective an adjunct as pethidine. With both drugs a proportion of patients exhibited repeated movements, breath-holding, and/or coughing on the tube. There was no significant difference in the respiratory effects of the analgesic drugs. The waking time in the group of patients given anileridine was significantly shorter than in those receiving pethidine. Anileridine was found to be 3.8 times as potent as pethidine.

Mark Swerdlow

397. The Effect of Intravenous Injections of Meperidine and Anileridine on Thiopental Requirement and Recovery Time

A. S. GALE. *Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.]* 39, 339-344, July-Aug., 1960. 1 fig., 10 refs.

The effect of pethidine and anileridine on the amount of thiopentone required and the recovery time was studied at Mount Sinai Hospital, Cleveland, in patients undergoing dilatation and curettage. Premedication was with 50 mg. of pethidine and 0.4 mg. of scopolamine. In all cases anaesthesia was induced with 60 mg. of thiopentone and maintained with nitrous oxide, oxygen, and further thiopentone as required. One minute before induction of anaesthesia 85 patients received pethidine intravenously in a dosage of 0.13 to 1.20 mg. per lb. (0.28 to 2.6 mg. per kg.) body weight and 60 patients received 0.04 to 0.16 mg. per lb. (0.08 to 0.3 mg. per kg.) body weight of anileridine; 108 patients did not receive a narcotic and served as controls.

With both narcotic drugs the amount of thiopentone required decreased approximately in proportion to the logarithm of the dose of the narcotic given. The recovery time was shorter with both narcotics than in the control group, but anileridine was the more effective. Recovery time was not further shortened by the larger doses of the narcotics.

Mark Swerdlow

398. Anileridine as a Supplement to Balanced Anaesthesia: Concentration in the Blood

D. H. HASELHORN and D. LIPPARD. *Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.]* 39, 345-351, July-Aug., 1960. 2 figs., 7 refs.

Anileridine was given as a supplement to anaesthesia in 876 patients aged 9 to 95 years at Harrisburg Hospital, Pennsylvania. Before or immediately after induction of anaesthesia with thiopentone an intravenous injection, usually of 10 mg., of anileridine was given and repeated as necessary. Anaesthesia was maintained on a light plane with an infusion of 0.5% thiopentone together with nitrous oxide, oxygen, and suxamethonium. Altogether 51 patients were anaesthetized in this way, but in later cases, because of the high incidence of respiratory depression, anileridine was administered together with either levallorphan (449 patients) or nalorphine (76 patients). A control group of 300 patients received no narcotic supplement. Less thiopentone was required per minute in the groups given a supplementary narcotic, whether an antagonist was also given or not. In further studies 33 patients received 25 mg. of anileridine intravenously; blood samples were taken 1, 3, and sometimes

5 minutes later and analysed colorimetrically. It was found that little anileridine remained in the blood 5 minutes after administration.

[No indication is given of the nature of the operations performed. The average duration of anaesthesia was appreciably shorter in the control group than in the groups given narcotics.]

Mark Swerdlow

399. Predicting Downward Temperature Drift during Hypothermic Anesthesia

C. A. HAMILTON. *Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.]* 39, 355-360, July-Aug., 1960. 3 figs., 11 refs.

The rate of drift of esophageal temperatures during equilibration is exponential and may be graphically reduplicated from an exponential equation. The extent of drift and the surgical hypothermia level of esophageal temperature are predictable by the method employed. It appears feasible for the anesthesiologist to predict the final level of drift simply by reference to a graph. This is done using data plotted from the first 10 to 15 minutes of cooling. The practical value of so doing should be evident in that it will permit earlier application of thermoregulatory measures if the predicted esophageal temperature is lower or higher than desired.—[Author's summary.]

400. Incidence and Prevention of Muscle Pain following the Administration of Succinylcholine

L. F. LAMOREAUX and K. F. URBACH. *Anesthesiology [Anesthesiology]* 21, 394-396, July-Aug., 1960. 8 refs.

Muscle pains often occur after administration of succinylcholine. Some workers have suggested that they may be related to the fasciculation often noted with this drug. Slow administration alone will not prevent the pains. At the United States Public Health Service Hospital, Staten Island, New York, 113 patients (male, aged 18 to 80 years) were divided into four groups and treated as follows: Group 1 received 50 mg. succinylcholine by rapid injection; Group 2 received a 0.2% solution of this drug by slow infusion; Group 3 were given 3 mg. of D-tubocurarine followed by rapid injection of 50 mg. of succinylcholine; and Group 4 received the same dose of tubocurarine followed by slow infusion of the 0.2% solution of succinylcholine.

Fasciculation was visible only in the patients in Group 1, pain being produced in 10 out of 25 patients. With slow infusion in Group 2 the incidence of pain was reduced to 14%, but in Group 4, in which the infusion was preceded by D-tubocurarine, there was no further reduction in the incidence of muscle pain. The patients in Group 3 had no muscle pains. It is suggested that D-tubocurarine "protects from muscle pain by preventing a portion of the injected succinylcholine from depolarizing the muscle fibres".

W. Stanley Sykes

401. The Anaesthetist's Assessment: Some Factors to be Considered at a Pre-operative Visit

O. P. DINNICK. *British Journal of Anaesthesia [Brit. J. Anaesth.]* 32, 543-553, Nov., 1960. 9 refs.

Radiology

402. A Cytological and Cytochemical Study of X-irradiated Human Testes

E. E. DESCHNER, R. HUGH, and E. GRUPP. *Military Medicine [Mil. Med.]* 125, 447-462, July, 1960. 15 figs., 26 refs.

The histological changes in tissue from human testis following irradiation were studied in 19 men, aged 57 to 81, who were to undergo bilateral orchidectomy for prostatic cancer and who received a single dose of irradiation (1,200 r.) to one testis or part of one at a specified number of hours before operation. The time interval before operation varied from 3½ hours to 10 days. The specimens obtained at operation were studied, irradiated tissue being compared with unirradiated tissue from the same patient. Sections were examined for alkaline and acid phosphatase, glycogen, acid mucopolysaccharides, deoxyribonucleic acid, ribonucleic acid, basic proteins, elastic tissue, fibrin and collagen, protein-tyrosine, protein-SS groups, protein-SH groups, and phospholipids. The techniques are described, and the cytochemical findings, cytological appearances, pathological data, and morphological and histological changes are discussed in detail.

E. Stanley Lee

403. Histo-pathological Changes in the Central Nervous System of Animals after General Irradiation with Gamma Rays in Large Doses. (Гистопатологические изменения в центральной нервной системе при общем воздействии на организм животных гамма-лучей в больших дозах)

A. F. ВІВІКОВА. *Журнал Невропатологии и Психиатрии [Zh. Nevropat. Psihiat.]* 60, 529-534, No. 5, 1960. 2 figs., 6 refs.

In these experiments 7 dogs were subjected to intensive γ -irradiation from a cobalt installation, two of them receiving 20,000 r., three 15,000 r., one 10,000 r., and one 5,000 r. They survived 18 and 20 hours, 26 to 28 hours, 20½ hours, and 87 hours respectively for the four levels of irradiation; necropsy was performed not more than 2½ hours after death and revealed the following lesions.

In all 7 animals there was extreme dilatation of the vessels of the spinal cord and the meninges, and in the brain substance. The intima was swollen in some cases, shrunken in others, and there was vacuolation and plasma infiltration of the vessel walls. Focal haemorrhages were rare, occurring most frequently in the dog which survived longest. The effect upon the nerve cells and fibres and on the glia was much more severe. But the most marked feature was the disturbance of circulation of the cerebrospinal fluid (C.S.F.), the excessive production of which led to increased intracranial pressure and cerebral oedema. Degenerative changes occurred in the ependyma, especially in the 3rd and 4th ventricles, and patches

of degenerated nerve cells were found in all layers of the cerebral cortex; cytolysis, with the nuclei being either pale or very deeply stained, was observed in some areas, while in others the cells were shrivelled and atrophied. Large, strongly basophil nuclei were observed in the cells of the 2nd and 3rd layers of the cortex and in the large pyramidal Betz cells. In dogs which received 15,000 and 5,000 r. cells in the deep layers of the cortex and in the pyramidal layer of the cornu ammonis showed swollen nuclei devoid of chromatin granules and giving the appearance of transparent cysts filled with fluid.

In the cerebellum there was massive death of Purkinje cells, with pyknosis and hyperchromatosis, this also extending to the dentate nucleus. Silver impregnation by Snesev's method revealed coarsening and agglutination of the argyrophil granules, especially in the cortex, while demyelination of the nerve fibres was observed in all parts of the brain and spinal cord, being focal in some and diffuse in others. There were also a few instances of degeneration of the axis cylinders. Such local or general demyelination has been described after irradiation with smaller doses, but appearing much later. The reaction of the astrocytes of the glia differed in various parts of the brain. In all the dogs, irrespective of the dosage, severe dystrophic changes were observed in the cortex, the cells being thinned, with swollen and sometimes fragmented dendrites. The fibrous astrocytes in the subcortical white matter were often hypertrophied, and in the perivascular astrocytes the dendrites were fragmented or torn from the vessel walls; in some places, however, they remained unchanged. More severe damage was found in the astrocytes of the grey matter of the subcortical nuclei, mid-brain, medulla, cerebellum, and spinal cord. The changes in the oligodendrites consisted mainly in swelling, but in the subcortical region focal destruction had taken place. It was impossible to distinguish any microglia.

These changes are difficult to explain on the grounds of vascular disturbances alone, since hypoxia from this cause would not be expected to produce such a degree of degeneration in so short a time. There seems to be no doubt that intense irradiation with γ rays produces a diffuse pathological change in the central nervous system itself, involving both ectodermal and mesodermal structures.

L. Firman-Edwards

404. Some Factors Altering the Severity of Acute Radiation Pneumonitis. Variation with Cortisone, Heparin, and Antibiotics

W. T. MOSS, F. J. HADDY, and S. K. SWEANY. *Radiology [Radiology]* 75, 50-54, July, 1960. 5 figs., 11 refs.

The authors of this paper from the Northwestern University School of Medicine and Wesley Memorial Hospital, Chicago, carried out a controlled investigation of the effect of several agents (steroids, heparin, and anti-

coagulants) on radiation-induced lung changes in rats, using total thoracic compliance as a parameter. The whole chest was irradiated through a single anterior field, irradiation being given with a 220-kV. Picker machine. Dose-time factors were varied. Compliance was measured on the curarized anaesthetized rat. After intubation the lung volume was increased by 1-ml. increments and the endotracheal pressure continuously measured. Pressure-volume curves were constructed. Irradiation alone produced a reduction in total thoracic compliance. This reduction was much less marked when 2.5 mg. of cortisone was given daily by intramuscular injection from the beginning of irradiation and continued for 42 to 50 days. Heparin in a dosage of 0.7 mg. daily by intramuscular injection was without effect. There was slight benefit from a combination of penicillin, streptomycin, and tetracycline. *M. Sutton*

405. The Relationship between Oxygen Tension of Inhaled Gas and the Severity of Acute Radiation Pneumonitis

W. T. MOSS and F. J. HADDY. *Radiology* [Radiology] 75, 55-58, July, 1960. 4 figs., 8 refs.

The effect on irradiated lungs of rats of varying the inspired oxygen pressure was studied by measuring the total thoracic compliance. The skin reaction was also observed. Increasing oxygen tension in the inspired air dramatically increased the severity of skin reactions. With 7% oxygen at atmospheric pressure 2,000 r. single-dose whole-chest irradiation usually produced a barely perceptible epilation. Such a dose with 100% oxygen at 40 pounds (18 kg.) pressure caused a severe moist reaction. The compliance was changed less by irradiation at the higher oxygen tension. The authors found that the adrenal glands were heavier in animals irradiated during inhalation of oxygen at high tension than in those in the low-oxygen-tension group. They suggest that the severe skin and bone-marrow reaction produced in the high-oxygen-tension group stimulate adrenal hyperplasia with increased production of endogenous cortisone and subsequent suppression of compliance changes.

M. Sutton

406. Treatment of Carcinoma of the Vulva with $^{182}\text{Tantalum}$ Radiotherapy. (Die interstitielle Radio-Tantal 182-Therapie des Vulvakarzinoms)

A. JACOB and G. DIETRICH. *Strahlentherapie* [Strahlentherapie] 112, 421-427, 1960. 6 figs., 1 ref.

At the Municipal Hospitals, Nürnberg, between 1954 and 1959 the authors have treated 22 cases of carcinoma of the vulva by means of the interstitial insertion of radioactive tantalum wire, and describe the method as follows. Straight lengths of wire, 0.5 mm. in diameter, were inserted about 1 cm. deep to the skin by means of sharpened cannulae, the implant extending for at least 3 cm. beyond the visible or palpable tumour. The projecting ends of the wires were bent towards the tumour for fixation. The implants remained in place for 2 to 3 weeks, according to the dosage required, and during this time the patients were allowed up and had no difficulties with bowel evacuation or micturition. The dose

to the vulval lesion was calculated, and a total dose of from 8,000 to 10,000 r. was aimed at. A higher dose was given in a few cases, but this resulted in necrosis of the skin. X-ray therapy to the groins was begun while the implants were still in place. The results are regarded as very satisfactory; 4 patients have died, 3 from recurrence of the tumour and one from cardiovascular disease, but the remainder are so far free of cancer. The authors point out that the procedure is not dangerous, is simple, inexpensive, and well tolerated by the patient.

E. Stanley Lee

RADIODIAGNOSIS

407. Coronary Arteriography: Development of a Method in Animals with Particular Attention to Physiologic Effects

S. W. NELSON, W. MOLNAR, A. CHRISTOFORIDIS, and C. BRITT. *Radiology* [Radiology] 75, 34-49, July, 1960. 9 figs., 19 refs.

In this paper from the Ohio State University Health Center, Columbus, the authors describe a technique of coronary arteriography in dogs based on their method of aortic valvulography. A total of 350 injections were given to 50 mongrel dogs. The right common carotid artery was selected as the point of entry for the catheter, which was then passed through the brachiocephalic trunk into the ascending aorta. Initially, the catheter was placed in position above the aortic valve by fluoroscopic control, but it was found that the position of the tip could be determined by the appearance of a rather vigorous to-and-fro movement as the catheter approached the aortic valve. If the catheter was passed into the descending aorta this movement was minimal and did not increase. The best simultaneous visualization of the left and right coronary arteries was obtained with a multiple-side-opening nylon catheter having a closed end, a length of 14 to 16 inches (35.6 cm. to 40.6 cm.), an inside diameter of 2.5 mm., and an outside diameter of 3.5 mm. This size of catheter allowed a No. 13 intravenous needle to be inserted into its proximal end and contrast medium to be injected rapidly without leakage. (A nylon, as distinct from a rubber, catheter is too stiff to allow it to be inadvertently inserted into the coronary vessel itself.) In an animal weighing 40 lb. (18 kg.) 20 to 30 ml. of 90% sodium diatrizoate ("hypaque") was necessary and was well tolerated; this is equivalent to 112 ml. in a human being weighing 68 kg. The stage of the cardiac cycle at which the injection was started did not appear to make any real difference and the injection was completed in approximately one second. Maximum concentration occurred in the coronary arteries during the second half of the injection and for one to two seconds afterwards. During this time, which was controlled electronically, 3 serial biplane radiographs were taken; it was also possible electronically to control simultaneous screening. The right coronary artery in dogs is small and visualization was not always entirely satisfactory, but it is thought unlikely that this will be the case in human beings. Significant electrocardiographic changes were not noted with this technique.

Of the 50 dogs, 7 died when large catheters were used necessitating open mediastinal manipulation; there were no deaths when the smaller catheters were used, nor did any deaths occur with injections of 20 to 30 ml. of 90% sodium diatrizoate when the number of injections was 3 or fewer.

John H. L. Conway-Hughes

408. Transcarotid Coronary Arteriography in Man with Emphasis on Inter coronary Arterial Anastomosis

W. MOLNAR, C. V. MECKSTROTH, S. W. NELSON, and R. W. BOOTH. *Radiology* [Radiology] 75, 185-196, Aug., 1960. 5 figs., 21 refs.

The technique of coronary arteriography as used clinically at the Ohio State University Health Center, Columbus, since 1958 and the radiological appearances of the coronary arteries in 50 patients are described. It is pointed out that the patients must be carefully selected and that the transcarotid approach should be avoided in those with carotid or cerebral vascular insufficiency and used with caution in arteriosclerotic patients over 60 years of age. Entry through the left common carotid artery is preferred if the innominate artery is tortuous or dilated. The risk of cerebral complications is increased in the presence of a thoracic aortic aneurysm and the prevention of mediastinal haemorrhage may be difficult in patients with haemorrhagic disease.

In the present series the shortest interval between myocardial infarction and coronary arteriography was 3 weeks except for one patient, who suffered no adverse effect. Describing the technique, the authors state that preliminary radiographs of good quality should be obtained and the x-ray field marked on the thorax. An exposure time of one-thirtieth of a second is preferable, with the lowest possible kilovoltage. Simultaneous filming and screening in two planes is desirable since the right coronary artery is best seen in the lateral plane and the left in the anteroposterior. If a double injection is considered risky and the examination is carried out in one plane the lateral view is to be preferred.

Since 1958 the authors have used 90% sodium diatrizoate in a total of 135 thoracic aortographic examinations and have not observed any major complications which could have been ascribed to the entry of the medium into the coronary vessels.

A closed-end, translucent, nylon catheter with 6 side holes around the distal centimetre and an outside diameter of 3.2 mm. and an inside diameter of 2.4 mm. is used. It is introduced under local anaesthesia, the correct position being determined by noting the increased amplitude of the transmitted pulsations as the catheter approaches the aortic valve. Both carotid arteries are compressed manually while 35 to 40 ml. of 90% sodium diatrizoate is introduced. Simultaneously with the beginning of the injection radiographs are taken at a rate of 4 per second for 4 seconds.

Of the 50 patients, 25 showed no evidence of coronary disease and served as controls. In all the controls there was good visualization of the coronary arteries and their branches, but among patients with coronary disease occlusion of the left coronary artery was seen in 3 cases and of the first centimetre of the right coronary

artery in 2 others. Inter coronary arterial anastomosis was demonstrated in one of these 5 patients and strongly suggested in another.

John H. L. Conway-Hughes

409. Percutaneous Retrograde Catheterization of the Left Ventricle and Systemic Arteries of Man

C. T. DOTTER and G. G. GENSINI. *Radiology* [Radiology] 75, 171-184, Aug., 1960. 11 figs., 18 refs.

The authors state that guided percutaneous arterial catheterization is superior to, and will no doubt supplant, translumbar aortography, and that it is the method of choice for demonstrating patent ductus arteriosus, coarctation, and other abnormalities affecting the aortic arch. It provides reliable means of studying aortic valvular disease and directly demonstrating the haemodynamic consequences of mitral insufficiency. As this simple and effective technique becomes more familiar its value in pelvic, abdominal, cerebral, and peripheral arteriography is increasingly recognized.

In this paper experience of this technique in 157 patients with cardiovascular disease is summarized. The method consists in the insertion of a needle into a systemic artery, usually the femoral, and passing through the needle a long, flexible, coil spring. The needle is withdrawn and polyethylene tubing is slid sleeve-wise along the spring and into the arterial lumen under fluoroscopic observation. General anaesthesia is not usually required. Rapid serial radiographs at 2 to 6 exposures per second are obtained. There were 2 deaths in the series: in a 2-year-old boy with tetralogy of Fallot cardiac arrest occurred during an apparently uneventful recovery from general anaesthesia, and in an elderly female with severe polyvalvular rheumatic disease ventricular fibrillation followed a supraventricular injection of contrast medium. There was a transient hemiplegia 8 hours after examination in a 9-year-old girl with transposed great vessels and a high interventricular septal defect. This was thought to be due to inadequate heparinization. In rare instances there was bleeding or haematoma formation at the site of injection.

The contrast media employed were 70% "urokon", 90% sodium diatrizoate ("hypaque"), and "ditriokon", a new iodine-containing medium which has the advantage of relatively low viscosity and requires no pre-injection warming. The numerous applications of the method are discussed and illustrated.

J. MacD. Holmes

410. Complications of Selective Angiocardiology

T. F. HILBISH and J. R. L. HERDT. *Radiology* [Radiology] 75, 197-206, Aug., 1960. 7 figs., 9 refs.

The complications of intracardiac angiocardiology are discussed with reference to experience in a series of 250 examinations carried out at the National Institutes of Health, Bethesda, Maryland. Under intravenous anaesthesia the injections of the contrast medium (70% "urokon") were forced through an intravascular or intracardiac catheter by means of a power-injection apparatus. The problem of backlash of the catheter within the heart during injection was largely resolved by replacing the open-end catheter by one with a closed

end and four side-wall holes. Cardiac arrhythmia frequently developed and pulmonary infarction occurred in 2 cases. Perforation of the heart with injection of contrast medium into the pericardium was a complication in one case, but surgical intervention resulted in recovery without apparent sequelae. Allergic reactions, which were not fatal, were noted in 5 cases, and there was hemiparesis with cortical blindness and bilateral deafness in one case. The most common radiological complication was extravasation of contrast material into the myocardium (6% of cases). Penetration of the myocardium by the catheter was seen in 3 cases and perforation of a presumed intact ventricular septum in one, but the only clinical reaction in these cases was a transient arrhythmia. In one case a small quantity of air was inadvertently injected into the left ventricle as a result of failure finally to check the power syringe; this patient had transposition of the great vessels so that the greater part of the air entered the pulmonary rather than the cerebral circulation with the result that there was no clinical reaction.

The authors emphasize that: (1) the examination should not be carried out on patients with unusual instability of the myocardium such as paroxysmal tachycardia; (2) the catheter should be moistened to avoid local irritation and thrombosis and manipulated gently to minimize endocardial trauma; (3) catheter position should be determined from radiographs in two planes; (4) adequate oxygenation is important; and (5) local anaesthesia may permit better oxygenation and patient control.

John H. L. Conway-Hughes

411. Radiological Identification of the Affected Segment in Circumscribed Tuberculosis of the Lung. (Röntgenologische Segmentdiagnostik der umschriebenen Lungentuberkulose)

H. SCHOLTZE and H. ST. STENDER. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [Fortschr. Röntgenstr.] 93, 44-53, July, 1960. 10 figs., 25 refs.

Writing from the University Radiological Clinic, Marburg, the authors point out that there are three methods which lead to the identification of the segment of lung involved in pulmonary tuberculosis: (1) tomography in several planes; (2) bronchography; and (3) selective angiography. (1) In tomography knowledge of the anatomy of the veins helps in the identification and separation of the various segments, as the veins tend to run close to the borders of the lung segments; it is specially in lateral tomograms that they can be clearly identified. Sometimes it is necessary to have slightly oblique projections. (2) Although there are no specific changes in the bronchogram, frayed edges are frequently seen, or narrowing of the contour. Sometimes the appearance resembles a string of beads. If there is cavitation, narrowing of the bronchus is practically always present, while if there is a tuberculoma the bronchus is frequently narrowed or obstructed. (3) With the aid of selective pulmonary angiography it is possible to fill individual arterial branches, and in this procedure it is partly the "capillary phase" which gives information about the state of the finer lung structure. In the healthy lung

there should be a fine, evenly distributed veil, which is missing when the lung is diseased, and the smaller arteries may also show changes and displacements.

Using all three methods in combination the authors have studied the segmental distribution of incidence of tuberculomata and cavities. Primary foci may occur anywhere in children, but in the adult they favour the apical and posterior lung segments. Epi-tuberculosis based on infected lymph nodes seems to be mainly located in segments of the mid-zone, while post-primary tuberculosis is most frequently found in the upper posterior segments.

F. M. Abeles

412. Soft Tissue Roentgenography. Its Use in Diagnosis of Thyroid Carcinoma

R. L. SEGAL, H. ZUCKERMAN, and E. W. FRIEDMAN. *Journal of the American Medical Association* [J. Amer. med. Ass.] 173, 1890-1894, Aug. 27, 1960. 2 figs., 16 refs.

It is not generally known that there is characteristic calcification in thyroid carcinoma, although this was described in 1958 by Holtz and Powers (*Amer. J. Roentgenol.*, 8, 997). The authors, working at Mount Sinai Hospital, New York, studied preoperative radiographs of the soft tissue of the neck in 6 patients who were later shown at operation to have carcinoma of the thyroid. In 3 cases typical calcification was found, agreeing in all essential respects with that described by Holtz and Powers.

Characteristically these calcifications are ill-defined, not dense, and without a calcific rim. They are easily distinguished from non-malignant calcification, which is sharply demarcated and denser. Lateral and oblique projections were taken to demonstrate the calcification, which, the authors state, presumably results from psammoma bodies in the thyroid. The sign is particularly valuable in the diagnosis of follicular or papillary carcinomata. Calcification was not seen in 23 patients with benign conditions.

D. E. Fletcher

413. Parietography of the Large Intestine. (La paretografia del grosso intestino)

G. C. CANOSI, M. DARDARI, and A. SANTINO. *Radiologia medica* [Radiol. med. (Torino)] 46, 631-648, July [received Sept.], 1960. 34 figs., 9 refs.

The authors describe, from the University of Modena, the technique of pneumoperitoneum followed by colonic insufflation. They point out that this should not replace the more conventional methods of examining the large intestine, but rather should supplement these in certain cases to obtain more precise information. Following insufflation, radiographic films are exposed in different positions, the exact nature of which necessarily depends on the area examined. The use of tomography is considered essential to separate the superimposed gas shadows, and a multi-layer cassette is also regarded as a necessity, otherwise the amount of gas present will vary in the different cuts. In cases in which the posterior wall of the colon is not covered by peritoneum air may be injected into the retroperitoneal space via the precoccygeal route, and this method can also be used for

rectal lesions, although the authors' experience here is limited to normal cases.

They claim that by means of parietography it is possible: (1) to confirm or exclude the presence of a neoplasm suspected after routine examination; (2) to demonstrate the extent of the neoplastic process in most cases; (3) to decide whether a neoplasm is inside or outside the lumen of the gut; (4) in certain cases to demonstrate abdominal metastases (hepatic, peritoneal, or lymphatic); and (5) to obtain further information concerning the benign or malignant nature of a neoplasm.

E. Giordani

414. Percutaneous Transhepatic Cholangiography in the Diagnosis of Posthepatic Jaundice

M. SANTOS, L. FIGUEROA, and O. LÓPEZ. *Surgery [Surgery]* 48, 295-303, Aug., 1960. 9 figs., 36 refs.

A technique of percutaneous transhepatic cholangiography is described. The patient lies flat on his back and a 12-cm. trocar and stylet are passed into the liver in the sagittal plane at an angle of 45 degrees from a point 3 cm. to the right of the midline and 3 cm. below the tip of the xiphisternum. Respiratory movements should stop as the abdominal wall is pierced, but may be resumed as soon as the trocar is in the liver. The stylet is then withdrawn, a 20-ml. syringe is attached, and constant suction is maintained. As soon as a main bile duct is entered large quantities of bile (10 to 300 ml.) are aspirated. After withdrawing as much bile as possible 35% diiodone is injected, and radiographs are then taken at different angles to avoid confusion from overlying shadows. In most cases 20 ml. of the contrast medium is sufficient, but occasionally 60 ml. is needed.

Over a number of years [unspecified] this examination has been carried out on 52 occasions in 46 patients at the Joaquín Aguirre Hospital, University of Chile, who had had jaundice for a period of "days to 4 years, with an average of 10 months and 15 days". In 6 cases a second puncture was needed, either because the first radiographs were poor or because the first puncture failed to reach a duct. In 5 of these 6 cases the second attempt was successful; there was only one double failure. Pain in the right upper quadrant occurred in all cases, but was rarely severe. [It is not stated whether it occurred on puncture or only when the contrast medium was injected.] Occasionally, the pain radiated to the right shoulder and was associated with spasm of the rectus; at subsequent operation no leakage of blood or bile could be found to explain this more extensive radiation. Shock, which responded to treatment, occurred in 2 cases; the cause of the shock was uncertain, but the radio-opaque solution was suspected. There were no fatalities, but bile peritonitis developed in one case, which was successfully treated by surgery. In 5 patients with cirrhosis the procedure failed; it also failed [for some undiscussed reason] in 3 cases of obstruction of the common bile duct. In 38 cases the information obtained was considered to be useful; in 5 of these the needle accidentally entered the gall-bladder, and in another a hydatid cyst was filled. Of 32 of the 46 cases in which the examination proceeded as planned,

choledocholithiasis was diagnosed in 14, "cancer of the biliary tract" in 11, benign stenosis of the common bile duct in 6, and inflammation of the sphincter of Oddi in one.

[There is no tabulation of cases or operation results to enable the reader to judge for himself the benefit to patients, and in this series there seem to have been no cases of epidemic hepatitis.]

Denys Jennings

415. A New Technique for Anaesthesia of the Phrenic Nerve in the Neck to Reduce Respiratory Movement of the Liver or the Spleen. (Nouvelle technique pour l'anesthésie du phrénique au niveau du cou avec immobilisation respiratoire du foie ou de la rate)

B. V. FUENTES, J. R. POLERO, and M. P. RUBINO. *Archives des maladies de l'appareil digestif et des maladies de la nutrition [Arch. Mal. Appar. dig.]* 49, 942-950, July-Aug., 1960. 5 figs., 3 refs.

Writing from the Faculty of Medicine, Montevideo, the authors describe a new technique for anaesthetizing the trunk of the phrenic nerve in the supraclavicular fossa, which they claim is superior to their previously used method in which the roots of this nerve were anaesthetized in the upper part of the neck. The new technique consists in the injection of 10 ml. of 2% lignocaine around the phrenic nerve as it lies under the aponeurosis of the scalenus anterior muscle. This operation can be performed on either side and the corresponding half of the diaphragm immobilized.

Since the main danger in hepatic and splenic puncture is the trauma resulting from respiratory movement of the liver or spleen against the puncture needle while it is held rigid by the abdominal or thoracic wall, it is hoped that the technique described will reduce to a minimum the risks inherent in such procedures as cholangiography by hepatic puncture, hepatic biopsy, either blind or at laparotomy, and splenography.

E. Giordani

416. Precipitation Pneumocystography Coupled with the Introduction of Gas into the Perivesical Cellular Tissue and Abdominal Cavity in the Diagnosis of Urinary Bladder Tumours. (Осадочная пневмоцистография в сочетании с введением газа в околопузырную клетчатку и полость брюшины в диагностике опухолей мочевого пузыря)

I. L. TAGER and V. M. PEREL'MAN. *Урология [Urologija]* 25, 24-26, July-Aug., 1960. 2 figs.

The authors describe a method of contrast cystography for the demonstration of tumour of the urinary bladder. Briefly, the technique is as follows: 100 to 150 ml. of a 15% suspension of barium is injected into the bladder and left for 20 minutes. The bladder is then washed out with a sterile solution, after which 200 to 600 ml. of oxygen is introduced into the perivesical tissues and 500 to 1,600 ml. of oxygen into the peritoneum. The bladder is now filled with oxygen and radiographs taken in various positions. The authors state that this method has proved valuable in diagnosing the extent of the tumour and the degree of its infiltration and is thus of considerable help in deciding the most appropriate form of treatment.

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